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## **Interventions for tobacco use cessation in people living with HIV and AIDS (Review)**

Pool ERM, Dogar O, Lindsay RP, Weatherburn P, Siddiqi K

Pool ERM, Dogar O, Lindsay RP, Weatherburn P, Siddiqi K.  
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# Interventions for tobacco use cessation in people living with HIV and AIDS

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## ABSTRACT

### Background

Tobacco use is highly prevalent amongst people living with HIV/AIDS (PLWHA) and has a substantial impact on morbidity and mortality.

### Objectives

To assess the effectiveness of interventions to motivate and assist tobacco use cessation for people living with HIV/AIDS (PLWHA), and to evaluate the risks of any harms associated with those interventions.

### Search methods

We searched the Cochrane Tobacco Addiction Group's Specialised Register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and PsycINFO in June 2015. We also searched EThOS, ProQuest, four clinical trial registries, reference lists of articles, and searched for conference abstracts using Web of Science and handsearched speciality conference databases.

### Selection criteria

Controlled trials of behavioural or pharmacological interventions for tobacco cessation for PLWHA.

### Data collection and analysis

Two review authors independently extracted all data using a standardised electronic data collection form. They extracted data on the nature of the intervention, participants, and proportion achieving abstinence and they contacted study authors to obtain missing information. We collected data on long-term (greater than or equal to six months) and short-term (less than six months) outcomes. Where appropriate, we performed meta-analysis and estimated the pooled effects using the Mantel-Haenszel fixed-effect method. Two authors independently assessed and reported the risk of bias according to prespecified criteria.

## Main results

We identified 14 studies relevant to this review, of which we included 12 in a meta-analysis ( $n = 2087$ ). All studies provided an intervention combining behavioural support and pharmacotherapy, and in most studies this was compared to a less intensive control, typically comprising a brief behavioural intervention plus pharmacotherapy.

There was moderate quality evidence from six studies for the long-term abstinence outcome, which showed no evidence of effect for more intense cessation interventions: (risk ratio (RR) 1.00, 95% confidence interval (CI) 0.72 to 1.39) with no evidence of heterogeneity ( $I^2 = 0\%$ ). The pooled long-term abstinence was 8% in both intervention and control conditions. There was very low quality evidence from 11 studies that more intense tobacco cessation interventions were effective in achieving short-term abstinence (RR 1.51, 95% CI 1.15 to 2.00); there was moderate heterogeneity ( $I^2 = 42\%$ ). Abstinence in the control group at short-term follow-up was 8% ( $n = 67/848$ ) and in the intervention group was 13% ( $n = 118/937$ ). The effect of tailoring the intervention for PLWHA was unclear. We further investigated the effect of intensity of behavioural intervention via number of sessions and total duration of contact. We failed to detect evidence of a difference in effect according to either measure of intensity, although there were few studies in each subgroup. It was not possible to perform the planned analysis of adverse events or HIV outcomes since these were not reported in more than one study.

## Authors' conclusions

There is moderate quality evidence that combined tobacco cessation interventions provide similar outcomes to controls in PLWHA in the long-term. There is very low quality evidence that combined tobacco cessation interventions were effective in helping PLWHA achieve short-term abstinence. Despite this, tobacco cessation interventions should be offered to PLWHA, since even non-sustained periods of abstinence have proven benefits. Further large, well designed studies of cessation interventions for PLWHA are needed.

## PLAIN LANGUAGE SUMMARY

### Interventions to help people living with HIV and AIDS to stop using tobacco

**Background:** Tobacco use is common amongst people living with HIV and AIDS (PLWHA); it causes a range of health problems and accounts for many deaths. There is good evidence about interventions to help people quit tobacco use in the general population, however the effectiveness in PLWHA was not known.

**Methods:** We reviewed the available evidence from trials to help PLWHA stop using tobacco. This evidence is correct up to June 2015. We conducted analyses of whether people were able to successfully quit tobacco use in the long-term (six months and over) and short-term (measured at less than six months).

**Results:** We found 14 relevant studies including over 2000 participants. All studies, except one, were conducted in the United States (US). All studies compared a behavioural intervention with medication, to a control group. The behavioural intervention was delivered via a range of methods including face-to-face, telephones, computers, and text messages. Nicotine replacement therapy or varenicline (medications that help tobacco users quit) was also given. Control participants typically received a less intensive, brief behavioural intervention, and the same medication as the intervention group. Six studies of moderate quality evidence investigated long-term abstinence; they did not show clear evidence of benefit of the more intense intervention. Eleven studies of very low quality evidence investigated short-term abstinence. The evidence suggested that a more intense intervention combining behavioural support and medication might help people to quit in the short-term.

**Quality of the evidence:** The quality of the evidence was judged to be moderate for the long-term abstinence outcome and very low for the short-term abstinence outcome, and so further research is needed to increase our confidence in our findings.

## SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [\[Explanation\]](#)

Tobacco use cessation in people living with HIV and AIDS						
<b>Patient or population:</b> consumers of tobacco living with HIV and AIDS <b>Setting:</b> All included studies conducted in USA <b>Intervention:</b> combined pharmacotherapy and behavioural support for smoking cessation <b>Comparison:</b> control						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with control	Risk with combined cessation intervention				
Proportion of participants abstinent - long-term (> 6 months) assessed via self report +/- biochemical verification	Study population		RR 1.00 (0.72 to 1.39)	1602 (6 RCTs)	⊕⊕⊕○ MODERATE <sup>1</sup>	
	80 per 1000	80 per 1000 (58 to 112)				
	Moderate					
	63 per 1000	63 per 1000 (46 to 88)				
Proportion of participants abstinent - short-term (> 4 weeks to < 6 months) assessed via self report +/- biochemical verification	Study population		RR 1.51 (1.15 to 2.00)	1785 (11 RCTs)	⊕○○○ VERY LOW <sup>1,2,3</sup>	
	79 per 1000	119 per 1000 (91 to 158)				
	Moderate					
	65 per 1000	98 per 1000 (75 to 130)				

\* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; RR: risk ratio.

#### GRADE Working Group grades of evidence

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

**Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

<sup>1</sup> Downgraded due to risk of bias. One study had high risk of reporting bias (although impact on results mitigated by obtaining unpublished data from study authors). Allocation concealment and blinding poorly described.

<sup>2</sup> Downgraded due to suspected publication bias indicated by asymmetrical funnel plot.

<sup>3</sup> Downgraded due to inconsistency. The direction of effect was not always consistent and moderate heterogeneity was present ( $I^2 = 42\%$ ).

## BACKGROUND

The introduction of combination anti-retroviral therapy (ART) has transformed HIV into a chronic disease (Deeks 2013), comparable to other long-term conditions such as diabetes (Nakagawa 2012). Once diagnosed, people living with HIV/AIDS (PLWHA) can have a near normal life expectancy (Nakagawa 2012). Causes of morbidity and mortality have changed; between 50% and 84% of deaths in PLWHA are now not AIDS-related (Ehren 2014; May 2013; Weber 2013), and rates of opportunistic infections have declined substantially over the past two decades (Buchacz 2010). Non-communicable diseases, particularly ischaemic heart disease and lung cancer, now represent a growing burden of disease in this population (May 2013).

The prevalence of tobacco consumption in PLWHA is substantial, and greater than that of the general population: between 47% and 65% of PLWHA smoke cigarettes (Friis-Møller 2003; Helleberg 2013; Miguez-Burbano 2005). Prevalence of tobacco use varies between countries, but there is evidence that PLWHA consume more tobacco than the general population in a range of contexts, from Zimbabwe to the United States (US) (Gritz 2004; Munyati 2006). Where ART is accessible, smoking results in greater loss of life years than the HIV infection itself in PLWHA who smoke (Helleberg 2013). In light of the high prevalence of smoking in combination with the changing trends in morbidity and mortality, smoking cessation has become highly relevant for this population.

### Description of the condition

Tobacco may affect the immune system of PLWHA, resulting in increased viral replication in macrophages, microglial, and T cells (Abbud 1995; Valiathan 2014). Valiathan and colleagues demonstrated that PLWHA who smoked had higher levels of immune exhaustion and impaired T cell functioning compared to both PLWHA non-smokers and HIV-negative smokers (Valiathan 2014).

Untreated HIV destroys CD4 cells (T4 lymphocytes expressing CD4 proteins), which play a central role in the immune system (Naif 2013; Simon 2006). In untreated HIV infection the 'CD4 count' (number of CD4 cells) gradually falls, increasing the risk of opportunistic infections and other complications (Naif 2013; Simon 2006). Treatment with ART aims to increase the CD4 count and to achieve viral suppression - to reduce the amount of HIV virus in the blood (the 'viral load') to an undetectable level. Smoking tobacco may affect the immune response to ART. Some evidence indicates that tobacco use might be associated with poorer ART outcomes including a lower likelihood of achieving viral suppression, and a higher likelihood of immunological failure (when CD4 count falls below the lowest point it had been prior to ART initiation) (Feldman 2006). However, cohort study data showed no difference in CD4 and viral load between smokers and non-smokers (Helleberg 2015).

Tobacco use causes substantial morbidity and mortality in PLWHA. The tobacco-related harm is substantially higher in PLWHA than smokers in the general population. Smoking was found to be attributable for 24.3% of all-cause mortality, 25.3% of major cardiovascular disease, 30.6% of non-AIDS-related cancer, and 25.4% of bacterial pneumonia amongst people living with HIV (Lifson 2010). This is partly due to a higher prevalence of tobacco use in PLWHA than the general population and partly due to their increased susceptibility to the impact of tobacco compared to other smokers. Lung cancer is the commonest non-AIDS-related cancer amongst PLWHA (May 2013), and compared to the general population, lung cancer occurs at a younger age and after shorter exposure to cigarettes (Winstone 2013). HIV has been identified as an independent factor for greater lung cancer risk (Sigel 2012). In addition, smoking is associated with increased incidence of a number of other cancers in PLWHA, including cancer of the anus and mouth (Bertisch 2013; Clifford 2005). Cardiovascular disease risk may be elevated in PLWHA, due to a combination of HIV viraemia, a pro-inflammatory state, and the association of some ART regimens with high cholesterol and impaired glucose tolerance (Friis-Møller 2003; Palella 2011). Tobacco use further increases cardiovascular risk, and cessation was found to be effective in significantly reducing this risk (Petoumenos 2011). Case-control studies show that the impact of smoking on acute coronary syndrome is nearly doubled for PLWHA who smoked compared to HIV-negative controls (Calvo-Sánchez 2013).

Amongst PLWHA who consume tobacco, incidence of oral lesions such as oral candidiasis and oral hairy leukoplakia are increased compared to non-users (Sroussi 2007). Current smokers are at significantly higher risk of bacterial pneumonia than non-smokers (Gordin 2008). The outcome of chronic obstructive pulmonary disease may be worse in PLWHA compared to HIV-negative people (Morris 2011). Smoking tobacco during pregnancy is an independent risk factor for adverse pregnancy outcomes for PLWHA, including small for gestational age, low birth weight and preterm birth (Aliyu 2013).

PLWHA who use tobacco are different from other tobacco users in several respects, which justifies a focused evidence review for smoking cessation in this population. PLWHA have been shown to have higher nicotine dependency levels than the general population and there is an increased prevalence of other co-dependencies, such as alcohol and illicit drugs (Benard 2007). This makes them more vulnerable to withdrawal symptoms on stopping tobacco use, and means sustained abstinence could be difficult to achieve. The prevalence of mental illness, particularly depression, in PLWHA is higher than that in the general population (Nurudtinova 2012; Schadé 2013), and is associated with a lower likelihood of quitting smoking and an increased likelihood of relapse after quitting (Weinberger 2012). Tobacco use was reported as a coping mechanism for general HIV-related symptoms and specifically for HIV-related neuropathy, depression, anxiety, and ART-associated lipodystrophy (Grover 2013; Reynolds 2004; Shuter 2012a). De-



spite the good prognosis of HIV, some PLWHA report fatalistic ideas and a pessimistic perception of their life expectancy, affecting their perceived susceptibility-associated risks of tobacco; one participant said: “If I live long enough to get cancer that’s great!” (Reynolds 2004).

Socioeconomic factors also have a substantial impact on tobacco use. Many PLWHA who use tobacco are members of one or more marginalised groups, including ethnic minorities, migrants, and men who have sex with men. Tobacco use was found to be consistently higher in lesbian, gay, bisexual, and transgender adults, compared to heterosexual adults in a range of countries (Marshall 2008), and they are also at higher risk of HIV. Additionally, in one study of PLWHA who use tobacco, two-thirds were found to be unemployed, almost half had an income under USD 10,000 per annum and more than one-third were in inadequate housing (Humfleet 2009). These factors may contribute to their continued tobacco use and reduce the likelihood of success in quitting. Social support networks are lacking for many PLWHA. In addition, some PLWHA who smoke, report that more than 40% of people in their social network are smokers, reinforcing their continued smoking (Humfleet 2009).

## Description of the intervention

In the general population, combined pharmacotherapy and counselling interventions are effective in achieving tobacco cessation (Stead 2016). PLWHA who are engaged in care, come into frequent contact with health professionals for regular tests and clinic appointments. This presents an opportunity to discuss and support cessation, but currently this opportunity is underutilised. HIV clinicians report a lack of confidence in initiating cessation therapies and insufficient time, despite recognising the importance (Horvath 2012; Shuter 2012b). Despite previous unsuccessful attempts to quit by over 80% of PLWHA who smoke (Shuter 2012a), a high proportion remain motivated to quit (Benard 2007; Shuter 2012a). The high prevalence of smoking, despite a substantial proportion expressing a desire to quit, reflects an unmet need for effective tobacco cessation interventions in PLWHA. There is need for clarity in how best to support PLWHA in tobacco cessation.

Tobacco cessation interventions may be brief advice, behavioural, pharmacological, or a combination. Behavioural support interventions may include group or individual counselling, consisting of appointments following the quit attempt where the smokers receive information, advice, and encouragement. Pharmacological interventions may include use of nicotine replacement therapy (NRT) via a range of modalities, as well as bupropion or varenicline. The literature on tobacco cessation suggests that individual pharmacotherapies are effective for tobacco cessation; however, these in combination with behavioural support are found to be more effective in the general population (Stead 2016). There is evidence of effectiveness of these tobacco cessation interventions

in the general population (Stead 2012; Stead 2016), but to our knowledge, there has not been an in-depth systematic review into their effectiveness in PLWHA.

## Why it is important to do this review

Tobacco use is highly prevalent and responsible for substantial morbidity and mortality amongst PLWHA (Helleberg 2013). It is therefore, important that health workers have the best available evidence to support PLWHA in their attempts to quit tobacco. A dedicated review of cessation interventions in PLWHA is justified as a number of relevant attributes of tobacco users with HIV/AIDS differ from those of other tobacco users. Furthermore, despite motivation to quit, PLWHA often find it difficult to achieve sustained abstinence.

## OBJECTIVES

Primary objective:

1. To assess the effectiveness of interventions to motivate and assist tobacco use cessation for people living with HIV/AIDS (PLWHA), and to evaluate the risks of any harms associated with those interventions.

Secondary objectives:

1. To assess whether interventions combining pharmacotherapy and behavioural support are more effective than either type of support alone in PLWHA.
2. To assess whether in PLWHA, tobacco cessation or cessation induction interventions tailored to PLWHA are more effective than ‘usual care’ non-tailored cessation interventions.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

1. Randomised controlled trials (RCTs).
2. Cluster-randomised controlled trials (cluster-RCTs).
3. Quasi-randomised controlled trials.
4. Other non-randomised controlled trials.

We did not exclude studies on the basis of language or publication status.

## Types of participants

We included trials of adults over 18 years who were HIV-positive. We included studies of all stages of HIV infection, and studies of men only, women only, and all genders.

Trial participants were consumers of tobacco. Had we located studies which differentiated between different types of tobacco users, we would have considered subgroup analysis.

## Types of interventions

We included interventions that targeted individuals. The interventions included behavioural and pharmacological elements. We did not locate any studies of cessation induction trials (typically brief advice by health professionals) that aimed to encourage future quit attempts by those tobacco users who were unwilling to give up at the time of recruitment.

We included interventions delivered via any format including telephone call, the Internet, and face-to-face. There was no restriction on the identity of the provider which included nurses, counsellors, and peers.

## Types of outcome measures

### Primary outcomes

The primary outcome measure is tobacco abstinence at a minimum of six months after the start of the intervention, referred to as long-term cessation. We did include trials with a shorter follow-up, but these did not contribute to the primary analysis. We recognise that measurement of cessation at six months or longer is optimal (West 2005); however we included a shorter-term outcome measure due to the relative paucity of research in the area of tobacco cessation for PLWHA. We assessed short-term abstinence as a secondary outcome measure and completed separate analyses for the short- and long-term follow-up periods.

We used the strictest definition of abstinence reported in the study, using sustained abstinence rates in preference to point prevalence, or floating prolonged abstinence. Definitions of sustained abstinence may allow for a small number of cigarettes during the period (West 2005). We preferred, but did not require, that abstinence was biochemically verified (for example, by exhaled carbon monoxide or serum, salivary, or urinary cotinine). We treated those participants lost to follow-up as continuing users of tobacco. These outcome measures are guided by the Russell Standards for smoking cessation trials (West 2005).

### Secondary outcomes

We assessed short-term abstinence as a secondary outcome measure. We required that the assessment point was at least four weeks, but less than six months, from the target quit date, or start of the intervention for studies of cessation induction.

In addition to short-term abstinence, we planned to look for data on the following secondary outcome measures: HIV viral load, CD4 count, and the incidence of opportunistic infections. We planned to extract data on and report any adverse effects.

## Search methods for identification of studies

### Electronic searches

The Tobacco Addiction Group's Trials Search Co-ordinator searched the Cochrane Tobacco Addiction Group's Specialised Register using terms related to the topic of HIV/AIDS, and the Cochrane Central Register of Controlled Trials (CENTRAL) combining topic-related and smoking cessation terms. We also searched MEDLINE, EMBASE, and PsycINFO, combining HIV topic terms with the smoking-related terms and study design limits, as used for the Specialised Register. The MEDLINE search terms are included in Appendix 1. All searches were carried out on the 17th June 2015. No other time period limitations were used.

### Searching other resources

We searched the grey literature as follows: theses and dissertations via EThOS and ProQuest. We looked for conference abstracts by searching the Conference Proceedings database in Web of Science and by handsearching the databases of the Society for Research on Nicotine and Tobacco, International AIDS Conference, and British HIV Association. We reviewed reference lists of literature reviews and consulted experts via email.

We searched for clinical trials via the US National Institutes of Health registry at [www.clinicaltrials.gov](http://www.clinicaltrials.gov), the World Health Organization (WHO) trials registry platform at [apps.who.int/trialsearch/](http://apps.who.int/trialsearch/), the European Union (EU) clinical trials register at [www.clinicaltrialsregister.eu](http://www.clinicaltrialsregister.eu), and the Pan African Clinical Trials Registry at [www.pactr.org](http://www.pactr.org). For unpublished trials identified via the registries, we attempted to contact authors and requested data for analysis.

## Data collection and analysis

### Selection of studies

Two review authors (EP reviewed all studies, RL and KS each reviewed a proportion) independently checked the title and abstracts of all retrieved records for relevance. Two authors (from EP, KS, and RL) then each reviewed the full-text reports of all studies not excluded based on title or abstract, and which were potentially eligible for inclusion. We resolved any disagreements regarding study inclusion through discussion with a third party (OD). We recorded the selection process in sufficient detail to complete a

PRISMA flow diagram (Moher 2009), and 'Characteristics of excluded studies' table.

### Data extraction and management

Two review authors (from EP, OD, and RL) extracted data using a standardised electronic data collection form. We then entered data into Review Manager 5 computer software for preparing Cochrane systematic reviews (RevMan 2014).

We extracted the following information, where available, for each study, in the [Characteristics of included studies](#) tables.

1. Methods: Study name (if applicable), study recruitment period, country, number of study centres, study setting, study recruitment procedure, study design.
2. Participants: N (intervention/control), definition of smoker used, specific demographic characteristics (e.g. mean age, age range, gender, ethnicity, sexuality), mean cigarettes per day, mean Fagerström Test for Nicotine Dependence (FTND) score, relevant inclusion criteria and exclusion criteria.
3. Interventions: Description of intervention(s) (treatment, dosage, regimen, behavioural support), description of control (treatment, dosage, regimen, behavioural support); what comparisons will be constructed between which groups, concomitant medications, and excluded medications.
4. Outcomes: Abstinence time points for long- and short-term analyses, definition of abstinence (e.g. sustained or point prevalence) at each point, biochemical validation, proportion of participants with follow-up data at each point. Other outcome reported (HIV viral load, CD4 count, incidence of opportunistic infections, adverse effects).
5. Notes: Source of funding for trial, and notable conflicts of interest of trial authors.

### Assessment of risk of bias in included studies

As recommended in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions*, we utilised the 'Risk of bias' tool within Review Manager 5 to assess the risk of bias for each included study (Higgins 2011; RevMan 2014). Two review authors (from EP, OD, and RL) independently assessed and reported the following information in the 'Risk of bias' table.

1. Method of random sequence generation.
2. Method of allocation concealment.
3. Blinding of participants, providers, or outcome assessors.
4. Numbers lost to follow-up or with unknown outcome, for each outcome used in the review, by intervention/control group.
5. Selective outcome reporting.
6. Any other threats to study quality.

We graded each trial as being at 'high', 'low', or 'unclear' risk of bias for each domain, and provided justification for our judgement in the table. We summarised the risk of bias judgements across different studies for each of the domains listed, and displayed the summary results in two 'Risk of bias' figures.

### Measures of treatment effect

We calculated a risk ratio (RR) for each cessation outcome for each trial included in the meta-analysis as follows: (number of participants abstinent from tobacco in the intervention group/ number of participants in the intervention group) / (number of participants abstinent from tobacco in the control group/number of participants in the control group).

### Unit of analysis issues

The unit of analysis is the individual level.

### Dealing with missing data

Where we identified missing data, we contacted the study authors to request missing data. We also contacted study authors if aspects of trial design or conduct were unclear.

We treated participants who have dropped out, or who were lost to follow-up, as continuing to use tobacco. We completed reanalysis, where possible, if study authors had not considered these participants as continuing to use tobacco. We noted the proportion of participants for whom data were missing in the 'Risk of bias' table.

### Assessment of heterogeneity

We evaluated levels of heterogeneity (study characteristics, methods, outcomes) between included studies to decide whether or not it is appropriate to pool the data, in two ways; firstly by checking if the confidence intervals (CIs) overlap. We used the  $I^2$  statistic to assess statistical heterogeneity, given by the formula  $[(Q - df)/Q] \times 100\%$ , where  $Q$  is the  $\chi^2$  statistic and  $df$  is its degrees of freedom (Higgins 2003). This describes the percentage of the variability in effect estimates that is due to heterogeneity rather than to sampling error (chance). A value greater than 50% may be considered to indicate substantial heterogeneity. The test has low power when used on a small number of studies (Higgins 2011).

### Assessment of reporting biases

Searching multiple sources (as detailed in the search strategies above) should reduce reporting biases. We avoided language bias by not limiting the search terms by language and used translation services where required. We did not exclude on the basis of publication status and aimed to minimise publication bias by inclusion of grey literature, conference abstracts, and the inclusion of data from unpublished trials identified from trial registries (Higgins 2011). However, this is dependent on the data being obtained.

We created a funnel plot with pseudo-95% confidence limits to identify possible publication bias for the secondary outcome of short-term cessation. We did not create a funnel plot for the primary outcome (long-term cessation) because we identified less than ten studies.

## Data synthesis

We extracted data from individual studies, reported them in table form, and completed a meta-analysis. We calculated quit rates based on numbers randomised to an intervention or control group. Where possible, we conducted intention-to-treat analyses, i.e. including all participants initially assigned to intervention or control in their original groups. We excluded from the denominators any deaths. We treated any other losses to follow-up as continuing tobacco users, as described above. We noted adverse events, serious adverse events, and deaths in the Results section.

Incidence of adverse events were poorly reported. It was therefore not possible to conduct a meta-analysis of the incidence of serious adverse events, taking those randomised as the denominator and including events up to thirty days after the end of treatment. It was also not possible to conduct a sensitivity analyses restricting the denominator to those known to have taken at least one dose of treatment/intervention as this figure was not reported.

For the meta-analysis, we pooled RRs using a Mantel-Haenszel fixed-effect model ((number of events in intervention condition / intervention denominator) / (number of events in control condition / control denominator)) with a 95% CI. Where the event is defined as tobacco cessation, a RR greater than one indicates that more people successfully quit in the treatment group than in the control group.

## 'Summary of findings' table

We created a 'Summary of findings' table for long-term abstinence outcomes (six months or longer) and short-term outcomes (greater than or equal to four weeks, but less than six months). We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of the body of evidence as it relates to the studies which contribute data to the prespecified outcomes. We used methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), using GRADEpro software (GRADEproGDT 2015). We justified all decisions to down- or upgrade the quality of the evidence using footnotes.

## Subgroup analysis and investigation of heterogeneity

We conducted subgroup analyses, to explore the impact of different variables on the findings of the review. This allowed us to identify and investigate unexplained sources of heterogeneity. We also completed subgroup analyses to compare the relative efficacy of the different interventions. We were unable to complete subgroup analysis to establish the effect of combined behavioural and pharmacological interventions versus single-focus interventions in PLWHA since all identified studies used combination interventions. We therefore added a post hoc objective to investigate the effect of intensity of the intervention.

We conducted additional subgroup analyses for each intervention-population-outcome association and study characteristics to explore sources of any heterogeneity, using the  $I^2$  statistic.

Only one study reported on the outcomes of HIV viral load and CD4 count. therefore, we did not calculate the RR or mean difference (MD).

We conducted subgroup analyses based on the provider of the behavioural intervention, mode of contact, participant selection, tailoring, number of sessions, and total duration of contact. The subgroups are as follows.

### Provider of behavioural intervention

- Healthcare professional
- Researcher
- Co-facilitation by a PLWHA peer and a health professional

### Mode of contact

- Face-to-face
- Telephone
- Text message
- Website/computer-based

Where the intervention was undertaken via more than one mode, the most frequently used mode was coded.

### Participant selection

- Selected for willingness or motivation to quit
- Not selected for willingness or motivation to quit

### Tailoring

- Intervention tailored for PLWHA
- Intervention not tailored for PLWHA

Where no tailoring was described, it was assumed that the intervention was non-tailored.

### Intensity

A post hoc objective involved analysis according to intensity of behavioural intervention. This analysis was undertaken using the same categories defined in a previous Cochrane review (Stead 2016), adapted from the US Guidelines AHRQ 2008. This involved analysis according to number of sessions and total duration of contact time. We used planned contact time and number of sessions where possible, if this was not reported or not clear, we used the reported average.

We categorised total contact time as follows.

- 0 (where support was provided by text message or website use alone)
- 1 to 30 minutes
- 31 to 90 minutes
- 91 to 300 minutes
- More than 300 minutes

We categorised number of person-to-person sessions as follows.

- 0 (where support was provided by text message or website use alone)
- 1 - 3 sessions
- 4 - 8 sessions
- More than 8 sessions

Intensity subgroup analyses were not completed for short-term outcomes because the planned contact may not have been completed at the time of short-term outcome assessment.

### **Sensitivity analysis**

We tested for small-study effects on the results of the meta-analysis performed.

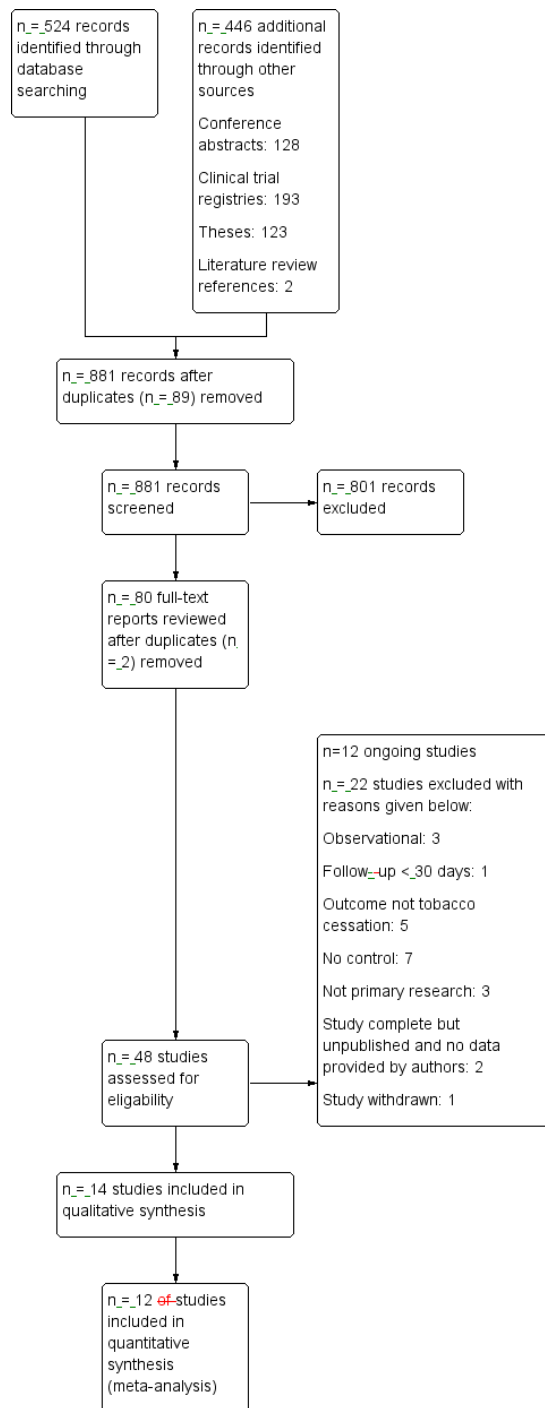
## **RESULTS**

### **Description of studies**

#### **Results of the search**

[Figure 1](#) contains a flow diagram detailing the search results. We identified 881 potentially relevant records; we identified some studies from more than one record. After screening and duplicate removal, we assessed 48 studies for eligibility and included 14 in the qualitative synthesis, 12 of which we included in a meta-analysis. The 22 studies that we excluded are listed in [Characteristics of excluded studies](#), and we judged 12 studies to be ongoing, which are summarised in [Characteristics of ongoing studies](#). We assigned the studies a study identifier (ID) based on the first author and year of the first major publication.

**Figure 1. Study flow diagram.**





## Included studies

Fourteen studies met the inclusion criteria and contributed to the review. We included all 14 studies in the qualitative synthesis, while 12 studies contributed to the quantitative synthesis. Six studies contributed to the analysis of long-term tobacco abstinence (the primary outcome) and 11 studies to short-term abstinence (the secondary outcome). Four studies reported both long- and short-term abstinence and we included them in both analyses.

The studies are described in detail in the [Characteristics of included studies](#) table. All studies were conducted after 2000, 13 of the 14 studies were conducted in the US, while one study, [Elzi 2006](#), was conducted in Switzerland. All studies combined a behavioural intervention with pharmacotherapy, therefore, we could not investigate the objective of single versus combined intervention in this review. As an alternative, we investigated the effect of level of intensity of counselling.

We included two three-arm studies ([Humfleet 2013](#); [Shelley 2015](#)). In both cases, the two intervention groups were not similar enough to warrant combining them to create a single group. For these two studies, we divided the control groups into two equal groups and made independent comparisons as follows: intervention one versus half of the control and intervention two versus half of the control. For [Humfleet 2013](#): computer-based intervention versus control and individual counselling versus control. For [Shelley 2015](#): text message versus control and text message + adherence-based therapy versus control. In the meta-analyses, the intervention groups are identified in the footnotes.

We did not include two studies in the meta-analysis ([Elzi 2006](#); [Ferketich 2013](#)). [Elzi 2006](#) was nested in the Swiss HIV Cohort Study (SHCS), the intervention group was not randomised, and it comprised participants who expressed an interest in quitting. Whereas, the control group was formed of all other smokers participating in the SHCS at the study site; they were therefore systematically different from the intervention group. Inclusion of this study in the meta-analysis resulted in substantial heterogeneity with an  $I^2 > 80\%$ . We did not include [Ferketich 2013](#) in the meta-analysis as this study compared two pharmacotherapies and was not in-keeping with the comparison of behavioural intervention versus less intense behavioural intervention, and did not have a control arm. The study compared 12 weeks counselling and varenicline, with 12 weeks counselling and nicotine replacement therapy (NRT). It was also non-randomised.

Sample size was variable with a high proportion of small studies; seven studies had a sample size of less than 150 participants ([Cropsey 2013](#); [Ingersoll 2009](#); [Manuel 2013](#); [Moadel 2012](#); [Shuter 2014](#); [Vidrine 2006](#); [Wewers 2000](#)).

## Participant characteristics

More than 1600 participants contributed to the meta-analysis for the primary outcome of long-term abstinence (six months or greater). An additional 485 participants contributed to the meta-analysis for the secondary outcome of short-term abstinence (greater than or equal to four weeks, but less than six months).

Sexual orientation and ethnicity were recorded inconsistently in different studies. Only six out of 14 studies reporting any measure of sexual orientation, despite the relevance of sexual orientation in studies of PLWHA. Where sexual orientation was described, approximately 35% to 50% of participants were homosexual. The overall proportion of homosexual participants ranged from 3% in [Manuel 2013](#) to 68% in [Humfleet 2013](#). Notably, the participants in [Manuel 2013](#) were all women.

Black or African American ethnicity was the modal category in eight studies. There were variations: from 95% of participants being Black in [Ingersoll 2009](#) to 53% White in [Humfleet 2013](#). The population of the only European study was 87% White ([Elzi 2006](#)). One study was specifically designed for the Latino community, and having a Latino/Hispanic ethnicity was an inclusion criterion of that study ([Stanton 2015](#)). The reported average age of study participants was approximately 35 to 50 years.

## Description of the intervention: behavioural

### Provider

Some degree of behavioural intervention was provided to the intervention group in all studies. We categorised the provider of the behavioural interventions as follows; healthcare professionals, researchers or co-facilitated by a peer and a professional. The intervention was provided by healthcare professionals in nine studies ([Elzi 2006](#); [Ferketich 2013](#); [Humfleet 2013](#); [Ingersoll 2009](#); [Lloyd-Richardson 2009](#); [Manuel 2013](#); [Shelley 2015](#); [Stanton 2015](#); [Vidrine 2012](#)), by a researcher or a graduate student in two studies ([Cropsey 2013](#); [Vidrine 2006](#)), and co-facilitated by a PLWHA ex-smoker peer alongside a professional in two studies ([Moadel 2012](#); [Wewers 2000](#)).

There was variation in the degree of detail to which the qualifications or experience of the individuals delivering the behavioural interventions was described. We therefore adopted a broad categorisation of 'healthcare professional', which included nurses, motivational interviewing clinicians, counsellors, psychologists, and health educators, irrespective of the detail provided on their counselling skills, experience, or qualifications. Likewise, while some studies described the academic qualifications of the researchers providing interventions, little detail was provided on their training or counselling experience.

In addition to the website intervention, the participants in the computer-based intervention group of [Humfleet 2013](#) also received a 45-60 minute face-to-face meeting, including discussion of a quit date. However, it is unclear if the provider was a clinician or a researcher, so this group was not included in the provider subgroup analysis. We attempted to contact the authors but were unable to clarify the intervention provider.

### Mode of contact

In most studies the behavioural intervention was delivered face-to-face or via telephone, often in combination. Two studies investigated computer- or web-based delivery, in which participants completed online modules ([Humfleet 2013](#); [Shuter 2014](#)). One study delivered the intervention entirely via text message ([Shelley 2015](#)). Additional resources were provided in most studies, such as written materials.

Nearly half of the intervention groups ( $n = 7/16$ , 44%) offered between four and eight face-to-face or telephone sessions, and a quarter ( $n = 4/16$ , 25%) offered more than eight ([Elzi 2006](#); [Ferketich 2013](#); [Vidrine 2012](#); [Wewers 2000](#)). Most of the studies with long-term follow-up planned to provide 91-300 minutes of total contact time. Categorisations were made according to planned duration of contact; actual contact time per participant may have been lower. These categories also do not account for time spent using web-based interventions or reviewing text messages.

### Tailoring

Eleven of the interventions were specifically tailored to PLWHA. This was achieved through a range of methods, including emphasising impact of tobacco on the immune system and facilitation by a HIV-positive ex-smoker peer. Some authors did not describe how the intervention was tailored in detail. In the text message group of [Shelley 2015](#), the text messages did not contain the words HIV or AIDS in order to ensure confidentiality, although the messages were designed to emphasise particular barriers faced by PLWHA, such as stress. We did consider this intervention tailored, but recognise that the degree of tailoring varies between studies. In the computer-based intervention in [Humfleet 2013](#), the authors did not explicitly state that the computer-based intervention was tailored, although it was described as modelled on the individual counselling intervention. The counselling intervention was targeted to the needs of HIV-positive smokers through focussing on the impact of smoking on HIV. We considered the computer-based intervention group likely to be tailored, and therefore included it in the tailored versus generic control subgroup.

### Description of interventions: pharmacotherapy

Nicotine replacement therapy (NRT) via patches and/or lozenges was offered or provided to the intervention groups in most studies. In [Shelley 2015](#) and [Ferketich 2013](#), varenicline was used instead.

No studies included bupropion in their protocol, possibly due to the potential drug-drug interactions with a number of anti-retroviral therapy (ART) drugs. In [Shuter 2014](#) only NRT administration was planned in the protocol, but some participants also received bupropion and varenicline off protocol, however, they were retained within their original groups for the ITT analysis.

### Description of controls

In most studies the control group received 'usual care', which typically comprised NRT or varenicline, brief advice, and written materials. In two studies, the participants in the control group received no behavioural input or pharmacotherapy ([Cropsey 2013](#); [Elzi 2006](#)).

In two studies, participants in the control group received enhanced standard care, with NRT alongside a counselling schedule involving multiple contacts ([Lloyd-Richardson 2009](#); [Stanton 2015](#)). Although in these studies the intervention was still more intense than the control.

### Other study characteristics

The vast majority of included studies were randomised controlled trials (RCTs). The [Ferketich 2013](#) study was not randomised; participants selected their own group (varenicline or NRT) but were encouraged by study staff to select varenicline, unless medically contraindicated. The [Elzi 2006](#) study was also not randomised; all cohort study participants who expressed an interest in quitting were allocated to the intervention group; the control group included the remaining cohort study smokers.

Study inclusion criteria differed on one key point: whether willingness or motivation to quit was explicitly required for inclusion in the study. Five studies did not refer to motivation or willingness to quit in their inclusion criteria ([Cropsey 2013](#); [Humfleet 2013](#); [Ingersoll 2009](#); [Lloyd-Richardson 2009](#); [Stanton 2015](#)). In [Elzi 2006](#), interest in quitting was required for the intervention group, but not for the control.

The outcome of cessation was self reported in all studies, which was biochemically verified in all except one study ([Elzi 2006](#)). Biochemical verification was achieved mostly through expired carbon monoxide. Most studies used a cut-off point of  $< 7$  parts per million (ppm) or  $< 10$  ppm, although the lowest cut-off point used was  $< 3$  ppm ([Cropsey 2013](#)). In this study no participants in the intervention or control groups achieved abstinence verified by this low cut-off point, although 22% of the intervention group did achieve abstinence at the  $< 10$  ppm cut-off point ([Cropsey 2013](#)). In keeping with our protocol, we used the most conservative estimate of abstinence ([Pool 2014](#)). Two studies used a combination of methods for biochemical verification; expired carbon monoxide and urine cotinine, or urine cotinine and nicotine levels.

Only three studies used the outcome measure of sustained abstinence. The most commonly used measure was 7-day point prevalence smoking abstinence (PPA). One study planned to measure



both 7-day PPA and sustained abstinence, but the data collected were insufficient to report sustained abstinence (Shuter 2014).

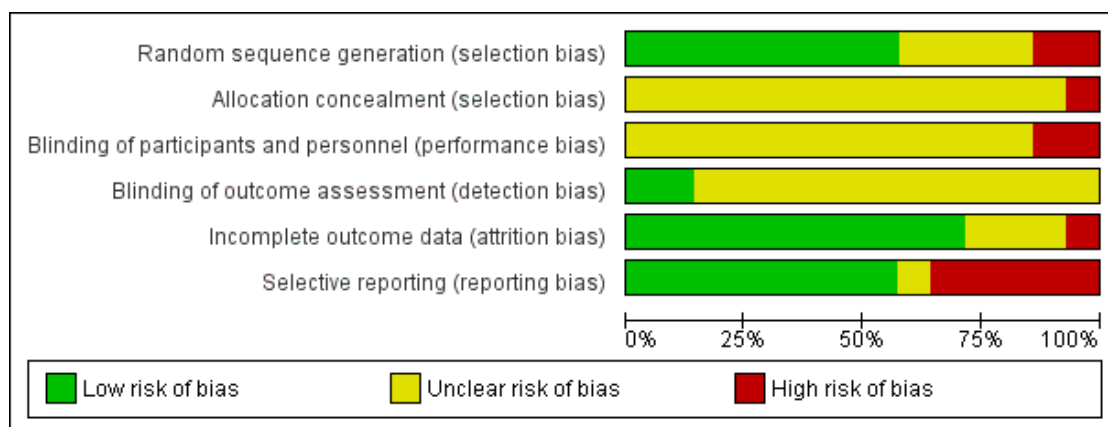
### Excluded studies

We list 22 studies as excluded. Reasons for exclusion can be found in the [Characteristics of excluded studies](#) table.

### Risk of bias in included studies

[Figure 2](#) and [Figure 3](#) present the review authors' judgements about each risk of bias item as percentages across all included studies.

**Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.**



**Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Cropsey 2013	+	?	?	?	?	-
Elzi 2006	-	?	?	?	+	+
Ferketich 2013	-	-	-	?	+	+
Humfleet 2013	+	?	?	?	+	-
Ingersoll 2009	?	?	?	?	?	-
Lloyd-Richardson 2009	+	?	?	+	+	+
Manuel 2013	+	?	-	+	-	+
Moadel 2012	+	?	?	?	+	-
Shelley 2015	?	?	?	?	?	?
Shuter 2014	+	?	?	?	+	-
Stanton 2015	+	?	?	?	+	+
Vidrine 2006	+	?	?	?	+	+
Vidrine 2012	?	?	?	?	+	+
Wewers 2000	?	?	?	?	+	+

## Allocation

Two studies reported non-randomised allocation and were therefore at high risk of bias for allocation concealment ([Elzi 2006](#); [Ferketich 2013](#)). All studies included in the meta-analysis were randomised. The method of allocation concealment was generally not described; only one study explicitly reported method of allocation concealment, but this was not in sufficient detail to permit judgement of bias.

## Blinding

Blinding of participants or personnel was not described in 12 out of 14 studies, and therefore the risk of these biases was unclear. In [Ferketich 2013](#), participants chose their group; we therefore judged this study to be at high risk of performance bias. In [Manuel 2013](#), a single provider delivered the counselling to both the intervention and control groups, therefore we judged that it was not feasible to blind the provider. Due to the nature of the behavioural interventions, it would have been difficult to blind providers to participant allocation in most studies.

Blinding of outcome assessment was only reported in detail in two studies ([Lloyd-Richardson 2009](#); [Manuel 2013](#)). In both studies, researchers blinded to the allocation status of the participant completed the outcome assessment and we therefore judged these studies to be at low risk of detection bias. In all other studies, risk of detection bias was unclear.

## Incomplete outcome data

We judged one study to be at high risk of attrition bias ([Manuel 2013](#)). In this study, one participant was lost to follow-up and no data were imputed for them (i.e. not considered missing = smoking). In addition, of the three participants who reported abstinence, biochemical testing for confirmation of abstinence was only performed on two specimens of urine, the reason for which was not explained. We considered the remaining studies to have low or unclear risk of attrition bias.

## Selective reporting

No study authors posted full study results on the clinical trial registries. We judged five studies to be at high risk of reporting bias. The outcome measures were not reported as described in the protocol in three studies ([Humfleet 2013](#); [Moadel 2012](#); [Shuter 2014](#)). In each study, the authors stated in the protocol that sustained abstinence and PPA outcomes would be assessed, however only reported PPA outcomes without explanation. Sustained abstinence data were obtained via communication with the authors for [Humfleet 2013](#), however PPA outcomes were used in the meta-analysis since the authors definition of sustained abstinence (defining relapse as seven consecutive days of smoking) means that PPA is the strictest definition of abstinence.

In [Ingersoll 2009](#), the design of the trial included two groups: intervention versus control. However, the study authors stated that there was no difference between the two groups and published only aggregated data, including baseline characteristics and outcome. We obtained per group data from the study author for inclusion in the analysis.

In [Cropsey 2013](#), the authors report measuring expired carbon monoxide and urine cotinine, but did not report these results.

## Other potential sources of bias

We did not judge any studies to be at risk of 'other' bias.

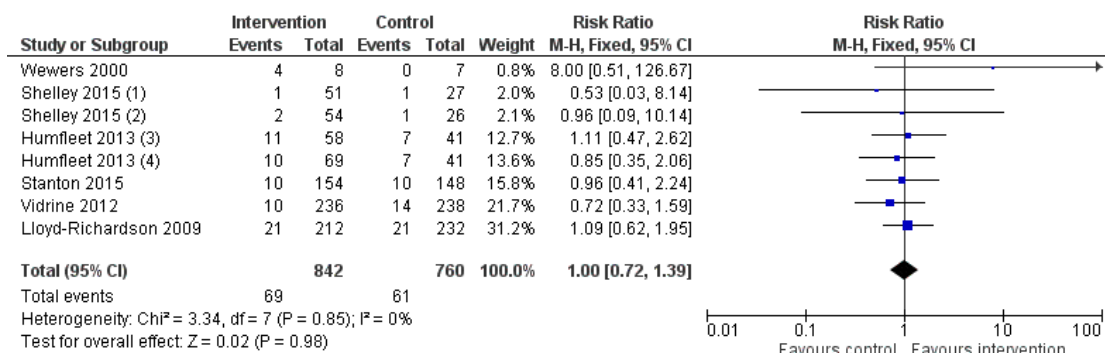
## Effects of interventions

See: [Summary of findings for the main comparison Tobacco use cessation in people living with HIV and AIDS](#)

## Long-term cessation

For long-term abstinence, a pooled estimate combining the six included studies showed no evidence of effect for the intervention (risk ratio (RR) 1.00, 95% confidence interval (CI) 0.72 to 1.39; moderate quality evidence) with no evidence of heterogeneity ( $I^2 = 0\%$ ) ([Analysis 1.1](#); [Figure 4](#); [Summary of findings for the main comparison](#)). Abstinence in the control group at long-term follow-up was 8% ( $n = 69/842$ ) and in the intervention group was also 8% ( $n = 61/760$ ).

**Figure 4. Forest plot of comparison: I Tobacco cessation intervention versus control, outcome: I.1 Proportion of participants abstinent.**



#### Footnotes

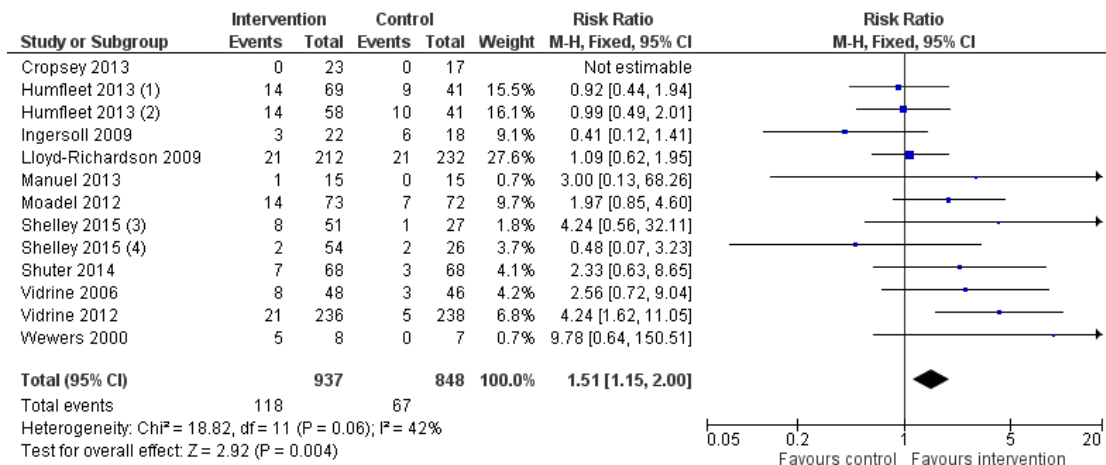
- (1) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)
- (2) Text messages versus Control (Control arm split between interventions to avoid double counting)
- (3) CBI versus Control (Control arm split between interventions to avoid double counting)
- (4) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

We did not create a funnel plot for the long-term outcome because fewer than 10 studies were included.

### Short-term cessation

For short-term abstinence, a pooled estimate of the 11 included studies showed benefit of intervention (RR 1.51, 95% CI 1.15 to 2.00; very low quality evidence) with moderate heterogeneity ( $I^2 = 42\%$ ) ([Analysis 2.1](#); [Figure 5](#); [Summary of findings for the main comparison](#)). Abstinence in the control group at short-term follow-up was 8% ( $n = 67/848$ ) and in the intervention group was 13% ( $n = 118/937$ ).

Figure 5.

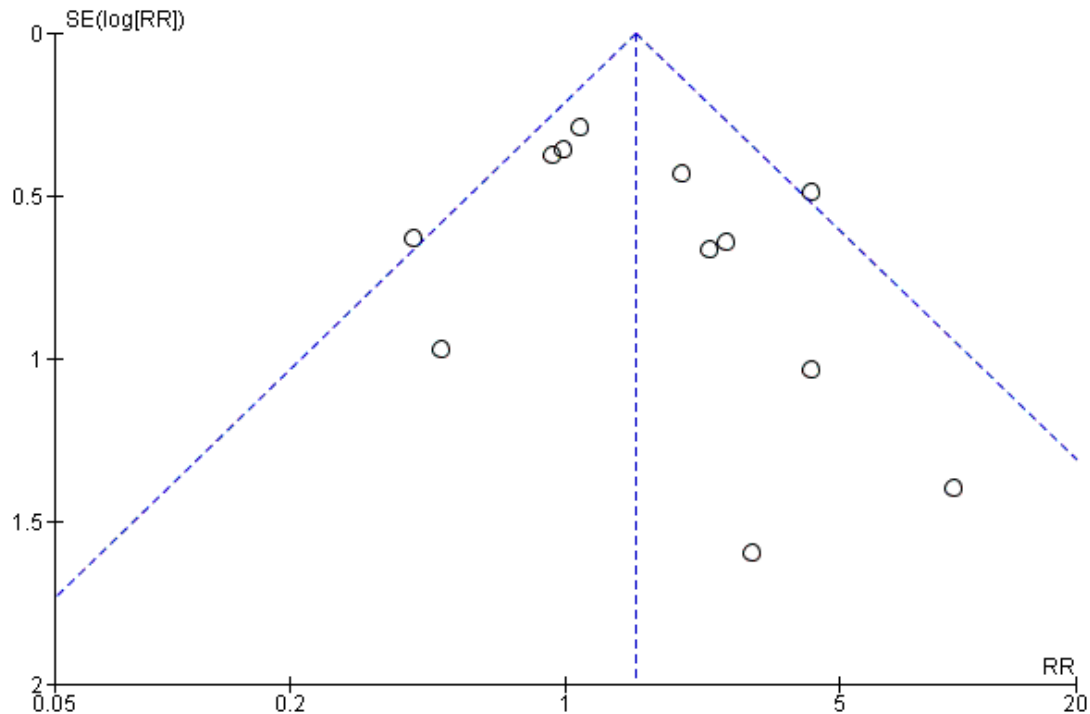


#### Footnotes

- (1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)
- (2) CBI versus Control (Control arm split between interventions to avoid double counting)
- (3) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)
- (4) Text messages versus Control (Control arm split between interventions to avoid double counting)

For the short-term outcome, a funnel plot showed some evidence of asymmetry, suggesting the possibility of publication bias (Figure 6).

**Figure 6. Funnel plot of comparison: 2 Tobacco cessation intervention versus control, outcome: 2.1 Short-term abstinence (4 weeks to < 6 months).**



We undertook a sensitivity analysis, removing smaller studies, and this did not significantly change the pooled estimate. We undertook a sensitivity analysis according to whether NRT or varenicline was given; it did not significantly change the pooled estimates for long-term or short-term abstinence ([Analysis 3.1](#); [Analysis 3.2](#)). Only one study included in the meta-analysis used varenicline ([Shelley 2015](#)). We undertook a further sensitivity analysis according to the degree of intervention provided to the control: no input, standard care, or enhanced standard care. Two studies provided enhanced standard care ([Lloyd-Richardson 2009](#); [Stanton 2015](#)); as may be expected the quit rate observed amongst controls was higher in these studies compared to controls receiving standard care or no input. For short-term outcomes, in the sensitivity analysis excluding these studies, the pooled estimate for the effect of the intervention increased slightly ([Analysis 4.2](#)). For long-term outcomes, the pooled estimate did not markedly change ([Analysis 4.1](#)).

### Subgroup analyses

#### Effect of provider

We categorised the provider of the behavioural intervention as follows: healthcare professional, researcher, or co-facilitation by a peer and professional ([Analysis 5.1](#)). We failed to detect evidence of a difference in the effect according to provider in the analysis for long-term abstinence. For short-term outcomes, the pooled estimate for interventions that were co-facilitated by a peer and professional (RR 2.52, 95% CI 1.14 to 5.56) were slightly larger than for other providers (healthcare professional alone: RR 1.41, 95% CI 0.98 to 2.03; and researcher: RR 2.56, 95% CI 0.72 to 9.04). However, the CIs overlapped.

#### Effect of mode of contact

We failed to detect evidence of an effect of subgroup categorisation by mode of contact for long-term abstinence ([Analysis 6.1](#)). For short-term outcomes, the pooled estimate was highest for interventions delivered via telephone (RR 3.69, 95% CI 1.80 to 7.53; [Analysis 6.2](#)). This was predominantly driven by the effect of one, large study ([Vidrine 2012](#)). There were few studies in some subgroups, which limits the conclusions possible from this subgroup analysis; only one intervention was delivered via text message ([Shelley 2015](#)), and two were delivered via computers

(Humfleet 2013; Shuter 2014).

### Participant selection

We failed to detect evidence of an effect of participant selection for long-term abstinence (Analysis 7.1). For short-term outcomes there is evidence of a difference in effect according to whether willingness or motivation to quit was required for participant inclusion (Analysis 7.2). The subgroup of participants who were selected for their willingness or motivation to quit had a higher pooled estimate of effect (RR 2.74, 95% CI 1.73 to 4.34,  $I^2 = 0\%$ ) compared to the subgroup for whom this was not required (RR 0.94, 95% CI 0.65 to 1.35,  $I^2 = 0\%$ ).

### Tailoring

All studies which reported long-term outcomes provided a tailored intervention, and one of these studies even tailored the control (Shelley 2015); therefore it was not possible to compare tailored to generic interventions for long-term abstinence (Analysis 8.1). For short-term outcomes, there was no strong evidence of a difference in effect for interventions tailored for PLWHA compared to generic interventions (Analysis 8.2). The comparison was limited due to the small number of studies providing a generic intervention. Only two studies provided a generic intervention, and in one of these, no participants in the intervention or control arm achieved abstinence at the level of biochemical verification set by the authors (Cropsey 2013).

### Intensity

The investigation of intensity of behavioural intervention, via number of sessions and total duration of contact for long-term abstinence, was a post hoc objective; we failed to detect evidence of a difference in effect according to either number of sessions or duration of total intervention (Analysis 9.1; Analysis 10.1). There were few studies in each subgroup. Intensity subgroup analyses were not completed for short-term outcomes because the intervention may not have been completed at the time of short-term outcome assessment.

### Adverse events

It was not possible to perform a quantitative synthesis of adverse events, since only one study reported them in detail (Ferketich 2013).

### HIV outcomes

It was not possible to perform the planned quantitative synthesis of HIV outcomes - CD4 count, viral load, and incidence of opportunistic infections - since only one study reported them (Elzi 2006).

## DISCUSSION

### Summary of main results

This systematic review provides evidence from 14 studies. More than 1600 participants from 12 studies contributed to the meta-analysis for the primary outcome of long-term abstinence.

In this review we found that more intense combined interventions of pharmacotherapy and behavioural support were effective in increasing the chance of achieving abstinence in the short-term (four weeks to less than six months) compared to a control group that typically included a single brief intervention and pharmacotherapy. The pooled estimate for short-term outcomes (risk ratio (RR) 1.51, 95% confidence interval (CI) 1.15 to 2.00) indicates that a combined intervention might typically increase cessation success by 15% to 100%. However, this effect was not observed for long-term abstinence (greater than six months).

There are differences between studies - in particular whether participants were selected for their willingness or motivation to quit. Those studies including only motivated or willing participants showed a larger pooled estimate of the effect of the intervention for short-term outcomes, although this was not observed at long-term follow-up.

As noted, we were unable to assess one of the original objectives - whether interventions combining pharmacotherapy and behavioural support were more effective than either type of support alone. This was because all included studies assessed a combined intervention compared to control. We added a post hoc objective assessing the effect of intensity of behavioural intervention. This analysis did not find any evidence of a difference in the effect of intensity. Although this subgroup analysis was limited by the small number of studies and does not definitively indicate that increasing the intensity would not result in an increased effect. In the general population, Stead 2016 also found no evidence that more intensive support increased the effect of treatment. Our analysis according to intensity only included personal contact time via telephone or in person. This may have underestimated the impact of interventions delivered via computers or text messages.

Subgroup analysis was undertaken according to whether the intervention was tailored for people living with HIV/AIDS (PLWHA). We failed to detect evidence of a difference in effect for tailored interventions for short-term abstinence, although this analysis was limited by a small number of studies providing a generic intervention. Subgroup analysis by tailoring was not possible for long-term outcomes because all studies provided a tailored intervention.

### Overall completeness and applicability of evidence

All studies included in the meta-analysis were undertaken in the US, although they do encompass a range of demographic profiles. There are health system and socioeconomic differences between

the US and Europe, as well as between the US and sub-Saharan Africa, where the majority of PLWHA live (UNAIDS 2015). This limits the generalisability of these results. Among ongoing studies, most are based in North America, although NCT01484340 is based in South Africa.

There remains a lack of studies which have large sample sizes and that assess long-term abstinence (greater than six months).

## Quality of the evidence

We evaluated the overall quality of the evidence according to GRADE criteria. For the primary outcome of long-term cessation, we judged the quality of evidence to be moderate. The quality of the evidence was downgraded due to risk of bias; one study was judged to be at high risk of reporting bias, and allocation concealment and blinding were poorly described.

For the secondary outcome of short-term cessation, we judged the quality of evidence to be very low due to inconsistency, in addition to reporting and detection biases.

We judged five studies to be at high risk of reporting biases where outcomes described in the protocol were not accounted for in the published reports. Although, in most cases communication with the study authors resulted in additional data being made available, or the study authors provided an explanation as to why they were unable to report the proposed outcomes. Allocation concealment and blinding were poorly described and therefore we assessed most studies to have 'unclear' judgements in these areas. There was also a high proportion of small studies, which reflects that this is a relatively new area of research. The rationale for upgrading or downgrading the quality of the body of evidence is presented in [Summary of findings for the main comparison](#).

## Potential biases in the review process

There is evidence of possible publication bias in the funnel plot for short-term outcomes, despite substantial effort being made to locate studies within the grey literature. Although we did identify some attrition bias and reporting bias, the impact of these were reduced through correspondence with authors to clarify points or request additional data. Additional data were kindly provided in most of these cases.

We added one objective post hoc - assessing the impact of intensity of the behavioural intervention on abstinence, and therefore potentially introducing some bias. However, we felt it was logical and consistent with the ethos of the original objective - to assess whether combined interventions are more effective than pharmacotherapy and behavioural support alone.

As is standard for Cochrane Reviews, all reports were reviewed and all data were extracted in duplicate in order to reduce bias.

## Agreements and disagreements with other studies or reviews

We believe that this is the first systematic review of tobacco cessation interventions for PLWHA to include meta-analysis. A previous systematic review provided a narrative overview and included some studies excluded by our stricter inclusion criteria (Moscou-Jackson 2014).

In the general population, interventions that combine behavioural and pharmacotherapy components have been shown to be effective for long-term abstinence when compared to a brief intervention without pharmacotherapy (Stead 2016), the reason for this effect not being observed in PLWHA is not clear. In the general population, tailoring cessation interventions has been shown to increase their effect (Hartmann-Boyce 2014). This was not shown in this review, but our comparison was limited by a small number of studies with a non-tailored generic intervention. It is important to consider that the evidence presented here is limited and has been judged to be of very low to moderate quality. There is much more and higher quality evidence assessing smoking cessation interventions and finding them effective in the general public. Therefore, it would be too premature to say that interventions aimed at the general population will not benefit PLWHA.

However, the following could explain a less pronounced effect. People living with mental illnesses have some similarities to PLWHA; they use more tobacco than the general population, often consume tobacco alongside drugs or alcohol, and may use tobacco to cope with their illness or treatment side effects (Tsoi 2013). In Tsoi and colleagues' review of smoking cessation interventions for people with schizophrenia they found that at short-term follow-up there was evidence in favour of a combined intervention (counselling and nicotine replacement therapy (NRT)) (Tsoi 2013), but long-term follow-up failed to detect evidence of a difference between the intervention and control. Their results echo the results of this meta-analysis and could reflect a higher potential for relapse in people with complex chronic diseases and multiple challenges. However, the comparison is limited, as the two populations have distinct differences, both medically and psychosocially.

## AUTHORS' CONCLUSIONS

### Implications for practice

The results of this review must be considered in the context of the small number of studies included and the low to moderate quality of the evidence, and it therefore should not be ruled out that smoking cessation interventions that have been found to work in the general population will not have an effect in PLWHA. More intense combined interventions of pharmacotherapy and behavioural support were shown to be effective in assisting PLWHA to achieve short-term abstinence, when compared to controls in



this review; however this effect was not observed at long-term follow-up. This could be a function of study biases. Therefore, evidence suggests that clinicians should offer a combined intervention to PLWHA who use tobacco, at least comprising a brief behavioural intervention with pharmacotherapy, since even non-sustained periods of abstinence have proven health benefits. The effects of tailoring, number of contacts and total duration of contact of behavioural support remain unclear.

## Implications for research

Further randomised controlled trials (RCTs) of tobacco cessation interventions in PLWHA are needed; they should include a large sample size and ensure that follow-up continues for at least six months, and preferably 12 months.

In this review, there was evidence of effectiveness of the intervention at short-term follow-up; however, we rated the quality of this evidence as 'very low' according to GRADE, and we did not observe any effect at long-term follow-up. Further research is needed to address the potential biases in the existing literature, including investigating relapse prevention in PLWHA who achieve short-term abstinence. This would maximise the probability of short-term success being translated into long-term abstinence.

Trials assessing the impact of tailoring and intensity of interventions are also needed. Data on sexual orientation should be rou-

tinely collected and reported in studies of PLWHA. Tobacco consumption may effect treatment response, as such, future studies measuring HIV outcomes - CD4 count, viral load, and incidence of opportunistic infections - would be highly informative. The fact that almost all studies are based in the US limits generalisability due to population and health system differences. Further studies should be based in a range of contexts, particularly in low- and middle-income countries with a high burden of HIV and tobacco consumption.

Future studies should ensure that reporting is in line with CONSORT criteria (Schulz 2010), particularly with regard to blinding and allocation concealment. None of the included studies reported their study in line with these criteria and as such, we judged many to be of 'unclear' risk of bias.

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\* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies [ordered by study ID]

#### Cropsey 2013

Methods	Country: US Design: paralell, pilot RCT Number of centres: 1 Selection: invited to participate during appointments Definition of tobacco user/smoker: self report $\geq 5$ cpd
Participants	Number: 40 participants Average age: 44.5 years Gender: 48% male Sexuality: not reported Race/ethnicity: 58% Black cpd: 19 cpd in intervention group, 15.5 cpd in control group Mean FTND score: 6.0 in intervention group, 6.5 in control group
Interventions	1. Intervention: one informational session for 20 minutes, delivered by a research assistant face-to-face. NRT, 14 mg patches and 2 mg lozenges for four weeks 2. Control: no intervention by research team Provider: research assistant (Bachelors level) Tailoring: neither intervention nor control were tailored for PLWHA
Outcomes	Abstinence: self reported PPA at 2, 4, and 8 weeks post-enrolment Validation: exhaled CO < or equal to 2 ppm
Notes	Cessation was not a primary outcome of the study. The cessation outcomes were not published but were obtained following correspondence with the author Funding: Centers for AIDS Research grant

#### *Risk of bias*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomised using a random numbers table
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Participants were asked questions and given questionnaires, the process is insufficiently described to permit judgement



Incomplete outcome data (attrition bias) All outcomes	Unclear risk	5 participants were excluded. The distribution of missing participants was balanced between groups (3:2) The reasons for missing data are insufficiently described to permit judgement
Selective reporting (reporting bias)	High risk	Biochemical verification of abstinence (by eCO and urine cotinine) was planned but not reported These data were obtained via communication with the author

**Elzi 2006**

Methods	Country: Switzerland Design: parallel, pilot controlled trial within Swiss HIV Cohort Study Number of centres: 1 Selection: participants who expressed an interest in quitting smoking were invited to participate; control group participants were smokers not interested in quitting Definition of tobacco user/smoker: self report $\geq 1$ cpd for $> 12$ months
Participants	Number: 417 (33 died, therefore excluded from final analysis) Average age: 43 years in intervention group, 40 years in control group Gender: 69% male Sexuality: not reported Race/ethnicity: 87% White cpd: 28 cpd in intervention group, 21 cpd in control group FTND score: $> 7$ for 74% in intervention group, not reported in control group
Interventions	1. Intervention: 15 individual face-to-face counselling sessions based on CBT. Sessions were 30 minutes duration and took place weekly during the first month, and monthly thereafter for 12 months. NRT patches, tablets, chewing gum, and sprays were offered to all participants; dose and duration not stated 2. Control: no intervention Provider: nurse trained in smoking cessation counselling Tailoring: the intervention was not described as tailored to PLWHA
Outcomes	Abstinence: self reported sustained abstinence at 12 months or greater Validation: no biochemical validation
Notes	This study was not included in the meta-analysis due to study design and heterogeneity Funding: the Swiss HIV Cohort Study is supported by the Swiss National Science Foundation Deaths: in the intervention group, 1/34 (3%) participants died of lung cancer. In the control group, 32/383 (8%) died during the study period. Of these deaths, 11 were HIV-related, including one related to lung cancer and one related to cardiovascular disease
<b><i>Risk of bias</i></b>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomised "participation in the programme [intervention group] was offered to those individuals who expressed an interest to quit smoking"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described in sufficient detail to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Smoking status extracted from routine clinic data, but clinician blinding not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	The distribution of missing participants was balanced between groups. Explanations were provided
Selective reporting (reporting bias)	Low risk	Primary outcome was reported in full

**Ferketich 2013**

Methods	Country: US Design: parallel, non-randomised controlled study, safety study Number of centres: 1 Selection: participants were recruited from within the Lung HIV study, interest in quitting was an inclusion criterion Definition of tobacco user/smoker: self report $\geq 5$ cpd
Participants	Number: 228 Average age: 43 years in intervention group, 43 years in control group Gender: 86% male in intervention group, 85% male in control group Sexuality: not reported Race/ethnicity: 61% White in intervention group, 50% White in control group cpd: 19.7 cpd in intervention group, 20 cpd in control group Mean FTND score: 4.9 in intervention group, 5.4 in control group
Interventions	1. Intervention: varenicline, titrated up to 1 mg twice daily. 12 weekly individual counselling sessions, first session face-to-face, all following sessions via telephone 2. Control: NRT 21 mg patch per day plus 4 mg gum as required to a maximum of 24 pieces per day. Counselling as per intervention group Provider: advanced practice nurse "experienced in delivering tobacco dependence treatment" Tailoring: neither intervention nor control were tailored for PLWHA

Outcomes	Abstinence: self reported 7-day PPA at 12 weeks post-initiation of treatment, TQD was set at approximately week 3, therefore abstinence assessment is approximately 9 weeks post-TQD Validation: eCO < 10 ppm for participants not using NRT, saliva cotinine < 15 ng/ml for participants using NRT
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Notes	Funding: National Institutes of Health grant This study was not included in the meta-analysis as it was designed to compare pharmacotherapy and was not in keeping with the comparison of intervention versus less intense control
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***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not randomised, "participants were encouraged to select varenicline" unless it was contraindicated in which case they were assigned to the control NRT group
Allocation concealment (selection bias)	High risk	Allocation was according to participant selection and not concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessed by face-to-face interview, insufficiently described to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Proportion of participants missing was approximately balanced between groups. Missing data imputed as missing = smoking
Selective reporting (reporting bias)	Low risk	Primary outcomes reported in full

## Humfleet 2013

Methods	Country: US Design: parallel, three-group RCT Number of centres: 3 Selection: participant self referral or clinician referral. Postcards and flyers at clinics, letters sent to patients Definition of tobacco user/smoker: self report smoking most days in a month
Participants	Number: 209 Average age: 45 years Gender: 82% male Sexuality: 62% Gay/Lesbian, 24.3% straight, 7.4% bisexual Race/ethnicity: 53% White Average cpd: 19.8 Mean FTND score: 4.9
Interventions	1. Computer-based intervention: one face-to-face orientation meeting of 45-60 minutes. Six counselling sessions based on CBT, delivered via a website, in addition to message board and 'ask the experts' options on the website. Mean duration on website 30-45 minutes. 10 weeks of NRT, patch or gum, available to participants who smoked $\geq 5$ cpd; dose not stated 2. Individual counselling: six individual, face-to-face sessions based on CBT over 12 weeks. Session duration 40-60 minutes. NRT as per Computer-based intervention group 3. Control: one-off, brief, face-to-face meeting with research staff and written reference guide provided. NRT as per the intervention groups Provider of individual counselling: "clinicians with a master's or doctoral degree in social work or psychology and had previous experience in smoking cessation treatment" Tailoring: individual counselling was tailored via focus on impact of smoking on HIV, stress, depression, low social support and HIV-related health issues. CBI was described as modelled on individual counselling and therefore assumed to be tailored. Control was not described as tailored
Outcomes	Abstinence: 7-day PPA and sustained abstinence at 12, 24, 26, and 52 weeks following intervention. In individual counselling group TQD was in week 2. TQD is not clearly described for CBI or control groups Validation: PPA outcomes were verified by eCO $\leq 10$ ppm, the sustained abstinence outcomes were not biochemically verified
Notes	PPA and sustained abstinence outcomes were measured but sustained outcomes were not described in detail in the published report. The sustained outcome data for meta-analysis were obtained via email communication with the authors Funding: NIDA grants and California TRDRP grant

### *Risk of bias*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were "randomized via computer algorithm to one of three conditions in 1:1:1 fashion into a parallel group de-

**Humfleet 2013** (Continued)

		sign”
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described in sufficient detail to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Proportion of missing participants was evenly balanced between groups
Selective reporting (reporting bias)	High risk	The study was registered on clinicaltrials.gov NCT00297453. The primary outcome measure of smoking cessation was measured by PPA and sustained abstinence, but sustained abstinence results were not reported in full

**Ingersoll 2009**

Methods	Country: US Design: parallel RCT Number of centres: 1 Selection: flyers and self referral or direct contact with researcher Definition of tobacco user/smoker: self report smoking daily
Participants	Number: 40 Average age: 42 years Gender: 55% male Sexuality: not reported Race/ethnicity: 95% Black Average cpd: 17.3 Mean FTND score: 5.0
Interventions	1. Intervention: one individual face-to-face counselling session, based on MI. NRT provided according to volume of tobacco consumed. If participants smoked > 10 cpd; 21 mg NRT patch for 1 month, 14 mg patch for 2 weeks and 7 mg patch for two weeks. If participants smoked < 10 cpd; 14 mg patch for 2 weeks and 7 mg patch for two weeks 2. Control: written materials to facilitate self assessment and tips for cessation. One-off face-to-face session where the materials were reviewed, but no counselling was provided. NRT as per intervention group Provider: post-doctoral fellow or counsellor Tailoring: the intervention was tailored through a focus on risk of smoking in the context of HIV. Control was not tailored for PLWHA

**Ingersoll 2009** (Continued)

Outcomes	Abstinence: self report PPA at 1 and 3 month follow-up Validation: eCO < 3 ppm
Notes	Additional data were obtained following correspondence with the author. In the published report the data from the two groups were added and presented as one data set Funding: NIH K01MH10688, NIH K23DA15774, and VCU's Institute for Drug and Alcohol Studies Conflicts of interest: Glaxo Smith Kline provided nicotine patches for the study

***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...participants were randomly assigned to one of two treatment conditions" but sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome was assessed by self report and eCO, process not described in sufficient detail to permit judgement of bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of participants (5) is reported but distribution is not described and explanations not given
Selective reporting (reporting bias)	High risk	The design was a two-group trial but the results were aggregated and only reported as a whole

**Lloyd-Richardson 2009**

Methods	Country: US Design: parallel RCT Number of centres: 8 (6 outpatient HIV clinics and 2 primary care centres) Selection: participants were recruited at their clinic Definition of tobacco user/smoker: self report $\geq 5$ cpd
Participants	Number: 444 Average age: 42 years Gender: 63% male Sexuality: not reported

	Race/ethnicity: 52% White cpd: 18.2 cpd Mean FTND score: 5.9
Interventions	1. Intervention: 1 brief advice session, plus 4 face-to-face individual counselling sessions based on MI and a quit day phone call. Duration of each counselling session was 30 minutes. Participants willing to set a TQD were provided with NRT patches, 8 weeks duration; dose not described 2. Control: 2 brief advice sessions, delivered face-to-face and self help written materials. In addition, participants willing to set a TQD received biweekly brief sessions (5 minutes duration) to reinforce quit effort, check patch side effects and distribute NRT patches. NRT provided as per intervention group Provider: health educator trained in smoking cessation Tailoring: Intervention was tailored via an emphasis on the impact on infections and immunity. Control was not tailored for PLWHA
Outcomes	Abstinence: 7-day PPA at 2, 4, and 6 months post-enrolment Validation: eCO < 10 ppm
Notes	The published report included percentage abstinence rate only; the number of participants abstinent were calculated as we were unable to obtain these via email correspondence with the authors Funding: NIDA grant, the National Heart, Lung, and Blood Institute grant, National Cancer Institute grant, an NIH-funded Transdisciplinary Tobacco Use Research Center Award grant, NIH-funded Lifespan/Tufts/Brown Center for AIDS Research Award, and by the Robert Wood Johnson Foundation

***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Patients were then randomized (using block randomization to ensure stratification by gender and level of motivation to quit smoking)"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described in sufficient detail to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Follow-up assessments were administered by research staff blinded to participant intervention assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Proportion of missing participants is balanced between groups. A missing = smoking assumption was used

Selective reporting (reporting bias)	Low risk	All of the primary outcomes were reported in full. A study protocol was published on clinicaltrials.gov (NCT00551720), the published method and outcomes correlate with the protocol methods and outcomes
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### Manuel 2013

Methods	Country: US Design: parallel RCT Number of centres: 1 Selection: participants were recruited at their clinic through flyers and clinician referrals. Participant interest in quitting was an inclusion criterion Definition of tobacco user/smoker: self reports of smoking daily for at least five of the last seven days
Participants	Number: 30 Average age: 49 years Gender: 100% female (being female was an inclusion criterion) Sexuality: 67% heterosexual Race/ethnicity: 47% Black cpd: 15.5 in intervention, 16.7 in control Mean FTND score: 4.1 in intervention, 5.0 for control
Interventions	1. Intervention: 1 face-to-face counselling session, based on MI. Average duration 27 minutes. Participants were referred to NRT programmes, but dose, duration and frequency of NRT not described 2. Control: 1 face-to-face session and written materials. Written materials were reviewed and strategies discussed. Duration not described. NRT as per the intervention Therapist: "highly experienced MI clinician" Tailoring: neither intervention nor control were tailored for PLWHA
Outcomes	Abstinence: 7-day PPA at 1 month follow-up Validation: urine nicotine and cotinine, scale not described
Notes	Funding: NIDA grant, the NIDA San Francisco Treatment Research Center grant, and University of California's Center for AIDS Prevention grant

### *Risk of bias*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A "permuted block randomization" technique was used
Allocation concealment (selection bias)	Unclear risk	Sealed envelopes were used but safeguards not described in sufficient detail to permit judgement: "the interviewer opened a



**Manuel 2013** (Continued)

		sealed envelope indicating which condition the participant had been randomized to receive"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not clearly described, but a single therapist delivered both control and intervention treatments therefore blinding is unfeasible
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"RA was blind to the participants' treatment condition"
Incomplete outcome data (attrition bias) All outcomes	High risk	1 participant lost to follow-up and no data imputed. Of the 3 people who reported abstinence, only two urine samples were taken, no explanation provided
Selective reporting (reporting bias)	Low risk	Primary outcomes are all reported

**Moadel 2012**

Methods	Country: US Design: parallel RCT Number of centres: 1 Selection: Participants were referred via clinicians or recruited in the waiting room, motivation to quit (> 6 on the readiness ladder) was required for inclusion Definition of tobacco user/smoker: self reported use of any product containing nicotine (cigarettes, pipes or cigars) in the past 5 days
Participants	Number: 145 Average age: 49 years Gender: 49% male Sexuality: not directly reported, HIV risk group was 'same sex contact' for 14.5% and 'heterosexual contact' for 57.9% Race/ethnicity: 86% Black cpd: 12.0 cpd Mean FTND score: 5.0
Interventions	1. Intervention: eight group counselling sessions of six to eight participants. Sessions were based on social cognitive theory principles and occurred weekly (90 minutes duration). Participants were offered three months of NRT; dose and mode of delivery not described 2. Control: one-off, face-to-face brief advice (< 5 minutes) to quit and written materials were provided. NRT as per intervention Provider: co-facilitated by one professional (psychology graduate student and ex-smoker) and one peer (PLWHA ex-smoker). Both "completed certified courses in tobacco treatment" Tailoring: intervention was tailored through use of a HIV-positive peer and highlighting the specific risks of smoking for PLWHA. The control was not tailored for PLWHA

**Moadel 2012** (Continued)

Outcomes	Abstinence: 7-day PPA at days 0, 42, and 132; assessment at 3 months from TQD Validation: eCO < 10 ppm
Notes	NRT was the only cessation medication offered to trial participants, although the authors report that some participants also obtained bupropion or varenicline outside of the study protocol Funding: NIH/NIDA grant, Clinical Core of the Center for AIDS Research at the Albert Einstein College of Medicine and Montefiore Medical Center funded by a NIH grant

***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Subjects who provided consent were randomized in a 1:1 schedule to the two study conditions"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described in sufficient detail to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	The distribution of missing participants was balanced between groups (4 from intervention and 2 from control). Missing data imputed as missing = smoking
Selective reporting (reporting bias)	High risk	The study was registered on clinicaltrials.gov NCT01106638. A secondary outcome measure of 'continuous abstinence' was described in the protocol but not reported

**Shelley 2015**

Methods	Country: US Design: parallel RCT Number of centres: 3 Selection: participants were recruited from HIV care centres, willingness to quit within the next two weeks was required for inclusion Definition of tobacco user/smoker: at least 5 cpd
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Participants	Number: 158 Participant characteristics are for 127 participants (outcome data are for all 158 participants) Average age: 50 years Gender: 84% male Sexuality: not reported Race/Ethnicity: 48% Black cpd: 15 cpd Mean FTND score: not reported	
Interventions	Intervention 1. Text messages : adherence-focused twice daily text messages. 12 weeks of varenicline. Based on Information Motivation Behaviour model Intervention 2. Adherence Behavioural Therapy : adherence-focused twice daily text messages, plus 7 sessions of telephone counselling. Planned duration of call: 20-30 minutes. Based on Information Motivation Behaviour model. 12 weeks of varenicline 3. Control/standard care: 12 weeks of varenicline, dose and frequency not reported. Information sheet and State Quitline number provided. Participants in intervention groups also received control Provider: trained counsellors (Masters level) Tailoring: text messages were tailored through conveying information considered particularly relevant to PLWH, but did not use the terms HIV/AIDS to ensure confidentiality. Adherence Behavioural Therapy intervention discussed the effects of smoking on HIV and focused on specific barriers for PLWH. The self help information sheet given as standard care was tailored to PLWH	
Outcomes	Abstinence: 7-day PPA at weeks 1, 4, 8, 12, and 24 from start of treatment Validation: eCO < 8 ppm	
Notes	The study was registered on clinicaltrials.gov NCT01898195 In published reports, 1 month per protocol outcomes were reported. 24 week intention-to-treat outcomes were obtained following correspondence with the author. Funding: NIDA and Centre for Drug and HIV Research Conflicts of interest: Pfizer provided study medication	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...participants were randomly assigned to one of two treatment conditions" but sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described

**Shelley 2015** (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Outcome assessed by self report and eCO. Proportion of missing participants not described per group. Overall, insufficiently described to permit judgement
Selective reporting (reporting bias)	Unclear risk	Outcome assessed by self report and eCO. Proportion of missing participants not described per group. Overall, insufficiently described to permit judgement

**Shuter 2014**

Methods	Country: US Design: parallel RCT Number of centres: one Selection: recruited at HIV clinic, interest in quitting was required for inclusion Definition of tobacco user/smoker: self reported use of cigarettes, pipes or cigars in the past five days
Participants	Number: 138 (2 died, therefore excluded from final analysis) Average age: 46 years Gender: 60% male Sexuality: not directly reported, HIV risk group was 'same sex contact' for 37% and 'heterosexual contact' for 44.2% Race/ethnicity: 60% Black cpd: 10.2 cpd in intervention, 11.5 cpd for control Mean FTND score: 4.8 in intervention, 4.9 in control
Interventions	1. Intervention: eight interactive web-based sessions, independently completed once a week, based on social cognitive theory. Mean time spent logged into the website; 59.8 minutes. NRT patches for three months were offered, dose and frequency not described 2. Control: brief advice (< 5 minutes duration) to quit and written materials. NRT as per intervention Provider: intervention was web-based Tailoring: the intervention was tailored to PLWHA through comparison of changes in HIV risk behaviour and smoking behaviour. Control was not tailored
Outcomes	Abstinence: 7-day PPA at 6 weeks and 3 months post-TQD Validation: eCO < 10 ppm
Notes	Draft report made available by authors prior to publication date Deaths: 2 participants died during the study period, 1 in control and 1 in intervention. Their deaths were not considered related to the study They were excluded in the reanalysis. Number abstinent were not reported (percentage

	abstinent were reported) in the publication, they were obtained via email communication with the author Funding: NIH/NCI grants, Clinical Core of the Center for AIDS Research at the Albert Einstein College of Medicine and Montefiore Medical Center funded by the NIH grant	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"... eligible subjects were randomized by study staff 1:1 into 2 conditions using a random number table and an even/odd allocation strategy"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described in sufficient detail to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessment was by self administered questionnaire and eCO. Not described in sufficient detail to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	The distribution of missing participants was balanced between groups (1 in intervention group, 3 in control group). Explanations were provided. Missing data imputed as missing = smoking
Selective reporting (reporting bias)	High risk	The methods in the report do not correlate with the protocol. The study was registered on clinicaltrials.gov NCT01570595. Primary and secondary outcomes differed in the published report compared to the protocol

**Stanton 2015**

Methods	Country: US Design: parallel RCT Number of centres: 9 Selection: clinician referral from immunology clinics Definition of tobacco user/smoker: self report smoking cigarettes in the past 7 days
Participants	Number: 302 Average age: 45 years

	Gender: 64% male Sexuality: not reported Race/ethnicity: 100% Latino (being Latino was required for inclusion) cpd and mean FTND score were not reported	
Interventions	1. Intervention: as per control plus two additional face-to-face individual counselling sessions (average duration of session 1: 62 minutes) and two additional ten minute phone calls, provided by health educator. All sessions culturally tailored to Latino. Option to bring a ‘support buddy’, culturally sensitive written materials and videos. If willing to set a TQD received NRT for 8 weeks, dose according to smoking level 2. Control: physician brief advice, plus two face-to-face individual counselling sessions and one quit day phone call (ten minutes), and written materials. NRT as per intervention Provider: health educator “at least Masters level professionals (or had equivalent years of clinical research experience) and were trained on the implementation of the manual driven interventions” Tailoring: the intervention was tailored being both a PLWHA and a Latino, emphasis on the specific health consequences of smoking on HIV. Control not tailored to PLWHA or Latino	
Outcomes	Abstinence: 7-day PPA at 6 and 12 months post-intervention Validation: eCO < 10 ppm	
Notes	Additional data and study design details were obtained via email communication with the authors ahead of full report publication Funding: NIDA grant	
<i>Risk of bias</i>		
<b>Bias</b>	<b>Authors’ judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Participants were randomised “using an urn randomisation procedure” and stratified by gender
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described in sufficient detail to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	The distribution of missing participants was balanced between groups (54 from control group, 68 from intervention group) . Missing data imputed as missing = smoking

Selective reporting (reporting bias)	Low risk	The study was registered on clinicaltrials.gov NCT00503230 and all primary outcomes were reported in full
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## Vidrine 2006

Methods	Country: US Design: parallel RCT Number of centres: 1 Selection: all patients screened at clinic appointments and invited if eligible. Willingness to set a quit date within 7 days was required for inclusion Definition of tobacco user/smoker: self report $\geq 5$ cpd and eCO $> 7$ ppm
Participants	Number: 94 (1 participant died, therefore excluded in reanalysis) Average age: 43 years in intervention group, 43 years in control Gender: 78% male Sexuality: not directly reported, HIV risk group was 'same sex contact' for 37.9% and 'heterosexual contact' for 35.8% Race/ethnicity: 72% Black cpd: 20.6 cpd in intervention group, 19.5 in control Mean FTND score: 5.5 in intervention group, 5.7 in control
Interventions	1. Intervention: eight counselling sessions over two months, plus access to a hotline. Delivered via cell phone and based on CBT. NRT patches provided for ten weeks. All intervention participants also received control 2. Control: one session of brief advice, face-to-face. NRT patches provided for ten weeks. Written materials; personal plan, self-help guide and tip sheet Provider: "research assistant (with a master's level qualification) trained in smoking cessation counselling" Tailoring: the intervention was tailored to PLWHA through emphasising the impact of smoking on the immune system and HIV-related diseases. Control tip sheet was tailored to PLWHA
Outcomes	Abstinence: self reported PPA and sustained abstinence Validation: eCO $< 7$ ppm
Notes	Funding: National Cancer Institute grant and the Margaret and James A. Elkins, Jr Faculty Achievement Award in Cancer Prevention 1 death reported in the control group. Reanalysis of data undertaken excluding this participant

## Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomised via "adaptive randomization designed to minimize imbalances in the distribution of prog-

**Vidrine 2006** (Continued)

		nostic factors (i.e. depression, number of cigarettes smoked per day, and level of nicotine dependence"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessed by face-to-face interview and eCO, the process was insufficiently described to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	The distribution of missing participants was balanced between groups (10 from intervention group, 8 from control group). Explanations were provided. Missing data imputed as missing = smoking
Selective reporting (reporting bias)	Low risk	Protocol not published, but all primary outcomes were reported in full

**Vidrine 2012**

Methods	Country: US Design: parallel RCT Number of centres: 1 Selection: patients screened at clinic appointments and invited if eligible, willingness to set a quit date within 1 week was required for inclusion Definition of tobacco user/smoker: self report $\geq 5$ cpd and eCO $> 7$ ppm
Participants	Number: 474 Average age: 45 years Gender: 70% male Sexuality: not directly reported, HIV risk group was 'men who have sex with men' for 46%% and 'heterosexual contact' for 25% Race/ethnicity: 77% Black cpd: 19.2 cpd Mean FTND score: 5.73 in intervention group, 5.82 in control group
Interventions	1. Intervention: 11 counselling sessions, based on CBT, delivered via cell phone, over 3 months. Plus access to a hotline and self help written materials. Instructions to obtain NRT patches, details of dose, frequency and duration not described. All intervention participants also received the control interventions 2. Control: 1 brief counselling session delivered face-to-face and self help written materials. NRT as per intervention Provider: "counsellors were trained and supervised by a licensed clinical psychologist"



**Vidrine 2012** (Continued)

	Tailoring: intervention was tailored to PLWHA through reinforcing the HIV specific benefits of abstinence. Control was not tailored
Outcomes	Abstinence: 7-day PPA and continuous abstinence at 3, 6, and 12 months post-enrolment Validation: eCO < 7 ppm
Notes	Only PPA outcomes were included in the published report, continuous abstinence outcomes were obtained via email communication with the authors Funding: NCI grant

***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...participants were randomized to 1 of 2 treatment groups"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome was assessed by self report using a computer and eCO. Process was not described in sufficient detail to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	The distribution of missing participants was balanced between groups (retention was 75.8% for the intervention group, and 78.2% for the control group). Missing data imputed as missing = smoking
Selective reporting (reporting bias)	Low risk	The study was registered on clinicaltrials.gov NCT00502827, all primary outcomes were reported in full

**Wewers 2000**

Methods	Country: US Design: parallel "quasi-experimental" controlled trial, pilot study Number of centres: 1 Selection: the study was advertised to clinic patients, interest in quitting smoking was required for inclusion Definition of tobacco user/smoker: self report $\geq 10$ cpd, for $\geq 1$ year
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Participants	Number: 15 Average age: 40 years in intervention group, 37 years in control Gender: 100% male Sexuality: not reported Race/ethnicity: not reported cpd: 27 cpd in intervention group, 28 cpd in control
Interventions	1. Intervention: three face-to-face individual counselling sessions (duration 30 minutes) and weekly phone calls (duration 10-15 minutes) over 8 weeks. Additional calls as required and written materials. NRT patches 21 mg for 6 weeks 2. Control: written materials and a letter with a strong quit smoking message Provider: peer educator (PLWHA ex-smoker) with a nurse as case manager. Peer was “trained by a nurse in smoking cessation treatment” Tailoring: the intervention was tailored through use of a HIV-positive peer educator, control was not tailored
Outcomes	Abstinence: PPA and continuous abstinence at 8 weeks and 8 months post-enrolment Validation: eCO < 8 ppm
Notes	Pilot study. Poor retention of control participants, retention rate at 8 months was 43% in control group and 88% in intervention group Funding: National Institutes of Health, National Institute of Allergy and Infectious Diseases, Adult AIDS Clinical Trials Group

### ***Risk of bias***

<b>Bias</b>	<b>Authors’ judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	“randomly assigned” but sequence generation not further described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not sufficiently described to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	The distribution of missing participants was unbalanced between groups, with high loss to follow-up in the control group at 8 months. However, since no control participants reported abstinence at 8 weeks, this would not have effected the outcome

**Wewers 2000** (Continued)

Selective reporting (reporting bias)	Low risk	No study protocol was published. But all primary outcomes were reported in full
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CBT: cognitive behavioural therapy

CO: carbon monoxide

cpd: cigarettes per day

eCO: expired carbon monoxide

FTND score: Fagerström Test for Nicotine Dependence score

MI: motivational interviewing

NRT: nicotine replacement therapy

PPA: point prevalence smoking abstinence

ppm: parts per million

PLWHA: people living with HIV/AIDS

RCT: randomised controlled trial

TQD: target quit date

**Characteristics of excluded studies** [ordered by study ID]

Study	Reason for exclusion
Berg 2014	Design: observational
Browning 2013	Design: review, not primary research
Burkhalter 2013	Outcome: not abstinence
Chefitz 2014	Outcome: not abstinence
Cui 2012	No control group
Cummins 2005	No control group
Fuster 2009	No control group
Huber 2012	Study design: observational
Lazev 2004	Follow-up: under 30 days
Lima 2009	No control group
Matthews 2013	No control group
McKie 1985	Not primary research

(Continued)

Mercie 2014	Study complete but unpublished. Author contacted, results not available
NCT01393301	Study complete but unpublished. Author contacted, results not available
NCT01436136	Multifactorial intervention. Primary outcome: not abstinence
NCT02029612	Study withdrawn
Pedrol-Clotet 2006	No control group
Reynolds 2009	Not primary research
Shadel 2014	Outcome: not abstinence
Shelley 2014	Outcome: not abstinence
Tornero 2009	No control group
Zwiebel 2008	Design: observational service review

### Characteristics of ongoing studies [ordered by study ID]

#### NCT00701896

Trial name or title	Smoking cessation using motivational therapy and varenicline
Methods	Open-label, non-randomised study
Participants	HIV-negative smokers and non-smokers, and HIV-positive smokers, in Ohio, US
Interventions	'Healthy control' HIV-negative non-smokers (no intervention) versus 'Healthy control' HIV-negative smokers (no intervention) versus 'Active comparator' HIV-positive smokers (varenicline, NRT) versus HIV-positive smokers (one motivational interview session)
Outcomes	"Develop and evaluate a specialized smoking cessation intervention" (outcome measure for evaluation not clearly documented) Lung function decline, the prevalence of respiratory symptoms and the occurrence/progression of emphysema
Starting date	June 2008
Contact information	Philip T. Diaz, Ohio State University
Notes	

**NCT01363245**

Trial name or title	Effectiveness of smoking-cessation interventions for urban hospital patients
Methods	Single-blind (outcome assessment) RCT
Participants	Hospitalised HIV-positive and HIV-negative adults in New York, US. Current smokers (smoked tobacco in last 30 days)
Interventions	Hospital telephone counselling versus faxed referral to Quitline
Outcomes	Abstinence at 6 and 12 months post-discharge, biochemically verified. Comparison of cessation outcomes between HIV-positive and HIV-negative participants
Starting date	July 2011
Contact information	Scott E. Sherman, NYU School of Medicine
Notes	

**NCT01484340**

Trial name or title	A smoking cessation trial in HIV-infected patients in South Africa
Methods	Open-label RCT
Participants	HIV-positive, current daily smokers (positive SmokeScreen test) in South Africa. Willing to set a quit date
Interventions	Intensive counselling versus intensive counselling + NRT
Outcomes	Abstinence at 2, 6, and 12 months. Biochemically verified by eCO < 8 ppm and urine cotinine
Starting date	March 2014
Contact information	Sandy Chon, <a href="mailto:schon2@jhmi.edu">schon2@jhmi.edu</a>
Notes	

**NCT01710137**

Trial name or title	A placebo controlled trial of varenicline for smoking among those with HIV/AIDS
Methods	Placebo controlled, double-blind, RCT
Participants	HIV-positive adults in Pennsylvania, USA. Current smokers (average at least 5 cigarettes per day)
Interventions	Varenicline + smoking cessation counselling versus placebo + smoking cessation counselling
Outcomes	Abstinence at 12 and 24 weeks, biochemically verified by urine cotinine

**NCT01710137** (Continued)

Starting date	October 2012
Contact information	Sonja Blazekovic, sonjab@mail.med.upenn.edu
Notes	

**NCT01800019**

Trial name or title	The Canadian HIV Quit Smoking Trial: tackling the co-morbidities of depression and cardiovascular disease in HIV+ smokers (CANQUIT)
Methods	Four-group RCT
Participants	HIV-positive, adults in Ontario, Canada. Current smokers (more than 5 cigarettes per day) and on anti-retroviral therapy with an undetectable HIV viral load
Interventions	NRT alone versus NRT and HIV tailored quit smoking counseling versus varenicline alone versus varenicline and HIV tailored quit smoking counseling
Outcomes	Abstinence at 48 weeks, biochemically verified by eCO < 10 ppm
Starting date	January 2014
Contact information	Louise Balfour, PhD. Ottawa Hospital Research Institute
Notes	

**NCT01886924**

Trial name or title	Computer-based MI to engage smokers living with HIV in tobacco quitline treatment
Methods	1) A pilot study to develop computer-based intervention; interviews 2) Preliminary RCT
Participants	HIV-positive, adults in Rhode Island, US. Current smokers (at least 10 cigarettes per day)
Interventions	Brief computer MI intervention to motivate tobacco quitline use versus computer-delivered nutrition education (control)
Outcomes	Outcomes of pilot study: feasibility and acceptability Outcomes of RCT: engagement in cessation treatment, number of quit attempts, PPA at 6 months
Starting date	February 2014
Contact information	Jacki Hecht, <a href="mailto:jhecht@butler.org">jhecht@butler.org</a>

**NCT01886924** (Continued)

Notes	
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**NCT01965405**

Trial name or title	Behavioral smoking cessation treatment for people living with HIV/AIDS
Methods	Open-label RCT
Participants	HIV-positive adult in Michigan, USA. Current smoker (more than 10 cigarettes per day)
Interventions	<b>Phase 1:</b> Brief counselling + bupropion versus brief counselling + bupropion + prize contingency management. <b>Phase 2 a:</b> allocation dependent on non-response in phase 1. Bupropion, continued counselling, monitored support to quit smoking versus bupropion, monitored support to quit smoking, prize contingency management for abstinence. <b>Phase 2 b:</b> allocation dependent on response in Phase 1. No additional treatment versus bupropion, continued monitoring and low intensity prize contingency management
Outcomes	Abstinence at 6 and 12 months, biochemically verified by urine cotinine and eCO
Starting date	August 2013
Contact information	Lisa Sulkowski, lsulkows@med.wayne.edu
Notes	

**NCT02072772**

Trial name or title	A trial of Positively Smoke Free group therapy for HIV-infected smokers
Methods	Open-label RCT
Participants	HIV-positive adult at one of two clinics in District of Columbia and New York, US. Current smoker and motivated to quit
Interventions	Positively Smoke Free (eight group therapy sessions led by a professional and a peer) + three months NRT versus standard care (brief advice and self help brochure) + three months NRT
Outcomes	Abstinence at 6 months, biochemically verified
Starting date	May 2014
Contact information	Jonathan Shuter, jshuter@montefiore.org
Notes	Linked to Moadel 2012 NCT01106638

**NCT02190643**

Trial name or title	Improving nicotine patch adherence among Latino HIV-positive smokers
Methods	RCT
Participants	HIV-positive, Latino smokers in US. Ready to set quit date
Interventions	Standard care: brief counselling + eight weeks NRT versus includes a module focused on brief counselling including a module focused on improving adherence + eight weeks NRT
Outcomes	Abstinence at 3 months biochemically verified
Starting date	August 2014
Contact information	Joan Tucker, jtucker@rand.org
Notes	

**NCT02302859**

Trial name or title	Mobile Media-Rich Interactive Guideline System (MMRIGS) pilot study
Methods	Open-label RCT
Participants	HIV-positive patients at one clinic in Texas, US. Smokers (at least 5 per day and at least 100 lifetime cigarettes) . Willing to make quit attempt within 1 week
Interventions	Standard care (brief advice, 8 sessions telephone counselling + 8 weeks NRT) versus automated treatment (brief advice + tailored video clips + 8 weeks of interactive text and graphical message via smartphone + 8 weeks NRT)
Outcomes	Abstinence at 3 months, biochemically verified by urine cotinine
Starting date	January 2015
Contact information	Alex Prokhorov, M.D. Anderson Cancer Center
Notes	

**NCT02432482**

Trial name or title	A mobile intervention to promote cessation in HIV-infected smokers
Methods	Open-label RCT
Participants	HIV-positive adults at one clinic in New York, US. Current smokers who are interested in quitting and own a smartphone



**NCT02432482** *(Continued)*

Interventions	Standard care: brief advice, written materials and offer of NRT versus mobile Positively Smoke Free (mPSF) providing 8 weekly sessions of audio/video messages, daily text messages + offer of NRT
Outcomes	Abstinence at 3 months, biochemically verified by eCO
Starting date	August 2015
Contact information	Jonathan Shuter, jshuter@montefiore.org
Notes	Linked to Shuter 2014 NCT01570595

**NCT02460900**

Trial name or title	Optimizing smoking cessation for people with HIV/AIDS who smoke
Methods	Double-blind, randomised placebo controlled trial
Participants	HIV-positive adults in US
Interventions	Varenicline + standard behavioural care versus placebo + standard behavioural care versus varenicline + Positively Smoke Free; tailored behavioural intervention versus placebo + Positively Smoke Free; tailored behavioural intervention
Outcomes	Abstinence at 24 weeks
Starting date	December 2015
Contact information	Seth S Himelhoch, shimelho@psych.umaryland.edu
Notes	

eCO: expired carbon monoxide

MI: motivational interviewing

NRT: nicotine replacement therapy

ppm: parts per million

RCT: randomised controlled trial

## DATA AND ANALYSES

### Comparison 1. Tobacco cessation intervention versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Long-term abstinence ( $\geq 6$ months)	6	1602	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.72, 1.39]

### Comparison 2. Tobacco cessation intervention versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Short-term abstinence (4 weeks to < 6 months)	11	1785	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [1.15, 2.00]

### Comparison 3. Subgroup by drug

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cessation at long-term follow-up	6	1602	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.72, 1.39]
1.1 NRT	5	1444	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.73, 1.42]
1.2 Varenicline	1	158	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.13, 4.38]
2 Cessation at short-term follow-up	11	1785	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [1.15, 2.00]
2.1 NRT	10	1627	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [1.13, 1.99]
2.2 Varenicline	1	158	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [0.49, 5.92]

### Comparison 4. Subgroup by control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Long-term cessation	6	1602	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.72, 1.39]
1.1 Standard care	4	856	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.61, 1.51]
1.2 Enhanced standard care	2	746	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.65, 1.69]
2 Short-term cessation	11	1785	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [1.15, 2.00]
2.1 No input	1	40	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Standard care	9	1301	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [1.21, 2.30]

2.3 Enhanced standard care	1	444	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.62, 1.95]
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### Comparison 5. Subgroup by provider

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cessation at long-term follow-up	6	1423	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.69, 1.41]
1.1 Health care professional	5	1408	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.64, 1.33]
1.2 Researcher	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Co-facilitated by peer and professional	1	15	Risk Ratio (M-H, Fixed, 95% CI)	8.0 [0.51, 126.67]
2 Cessation at short-term follow-up	10	1470	Risk Ratio (M-H, Fixed, 95% CI)	1.63 [1.19, 2.23]
2.1 Healthcare professional	6	1176	Risk Ratio (M-H, Fixed, 95% CI)	1.41 [0.98, 2.03]
2.2 Researcher	2	134	Risk Ratio (M-H, Fixed, 95% CI)	2.56 [0.72, 9.04]
2.3 Co-facilitated by peer and professional	2	160	Risk Ratio (M-H, Fixed, 95% CI)	2.52 [1.14, 5.56]

### Comparison 6. Subgroup by mode of contact

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cessation at long-term follow-up	6	1602	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.72, 1.39]
1.1 Face-to-face	2	554	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.63, 1.65]
1.2 Telephone	2	552	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.33, 1.50]
1.3 Computer	1	99	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.47, 2.62]
1.4 Text message	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.09, 10.14]
1.5 Equal face-to-face and telephone	2	317	Risk Ratio (M-H, Fixed, 95% CI)	1.31 [0.61, 2.82]
2 Cessation at short-term follow-up	11	1785	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [1.15, 2.00]
2.1 Face-to-face	6	809	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.77, 1.61]
2.2 Telephone	3	646	Risk Ratio (M-H, Fixed, 95% CI)	3.69 [1.80, 7.53]
2.3 Computer	2	235	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.68, 2.34]
2.4 Text message	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.07, 3.23]
2.5 Equal face-to-face and telephone	1	15	Risk Ratio (M-H, Fixed, 95% CI)	9.78 [0.64, 150.51]

**Comparison 7. Subgroup by selection**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cessation at long-term follow-up	6	1602	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.72, 1.39]
1.1 Selected for motivation/willingness to quit	3	647	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.49, 1.84]
1.2 Motivation/willingness to quit not required for inclusion	3	955	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.70, 1.49]
2 Cessation at short-term follow-up	11	1785	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [1.15, 2.00]
2.1 Selected for motivation/willingness to quit	7	1052	Risk Ratio (M-H, Fixed, 95% CI)	2.74 [1.73, 4.34]
2.2 Motivation/willingness to quit not required for inclusion	4	733	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.65, 1.35]

**Comparison 8. Subgroup by tailoring**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cessation at long-term follow-up	6	1602	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.68, 1.31]
1.1 Tailored intervention versus generic control	5	1444	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.68, 1.33]
1.2 Tailored intervention versus tailored control	1	158	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.13, 4.38]
1.3 Generic intervention versus generic control	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Cessation at short-term follow-up	11	1785	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [1.10, 1.91]
2.1 Tailored intervention versus generic control	7	1463	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [1.02, 1.83]
2.2 Tailored intervention versus tailored control	2	252	Risk Ratio (M-H, Fixed, 95% CI)	2.07 [0.86, 5.01]
2.3 Generic intervention versus generic control	2	70	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 68.26]

**Comparison 9. Subgroup by number of sessions**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cessation at long-term follow-up	6	1602	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.72, 1.39]
1.1 0 sessions	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.09, 10.14]
1.2 1 session	1	99	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.47, 2.62]
1.3 4 - 8 sessions	4	934	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.65, 1.50]
1.4 > 8 sessions	2	489	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.48, 2.01]

**Comparison 10. Subgroup by total contact time**

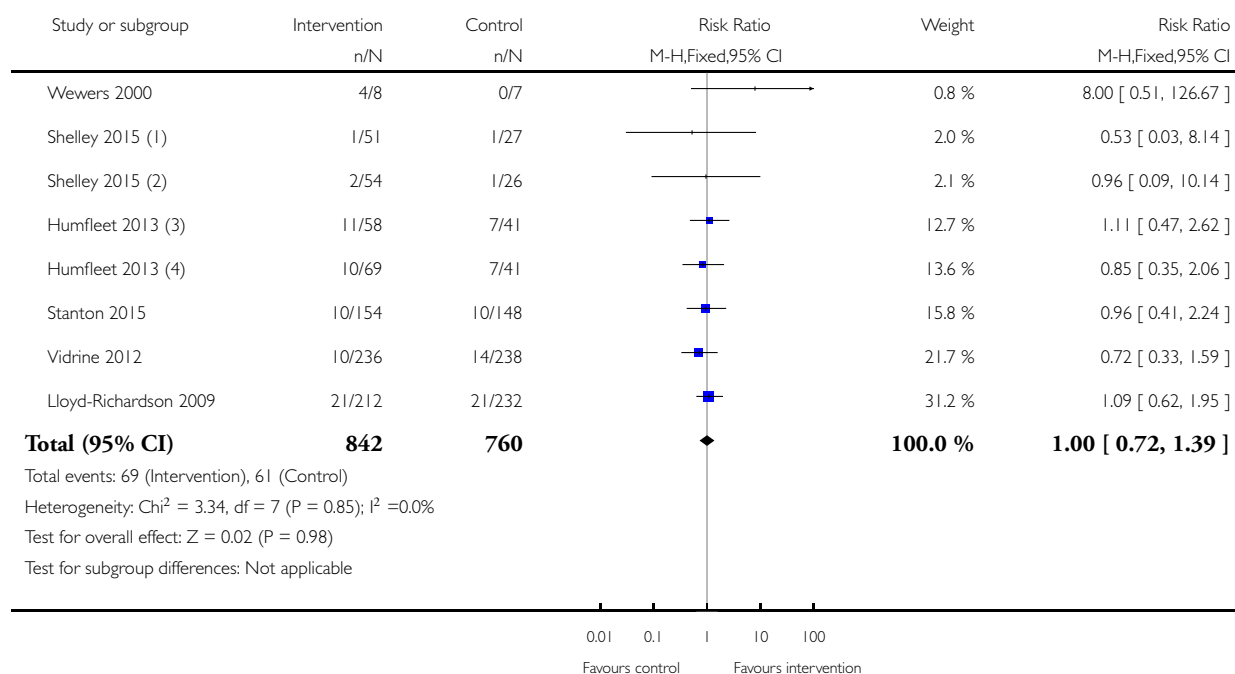
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cessation at long-term follow-up	5	1128	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.75, 1.55]
1.1 0 minutes	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.09, 10.14]
1.2 1 - 30 minutes	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 31 - 90 minutes	1	99	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.47, 2.62]
1.4 91 - 300 minutes	4	839	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.73, 1.80]
1.5 > 300 minutes	1	110	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.35, 2.06]

### Analysis 1.1. Comparison 1 Tobacco cessation intervention versus control, Outcome 1 Long-term abstinence ( $\geq 6$ months).

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 1 Tobacco cessation intervention versus control

Outcome: 1 Long-term abstinence ( $\geq 6$  months)



(1) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

(2) Text messages versus Control (Control arm split between interventions to avoid double counting)

(3) CBI versus Control (Control arm split between interventions to avoid double counting)

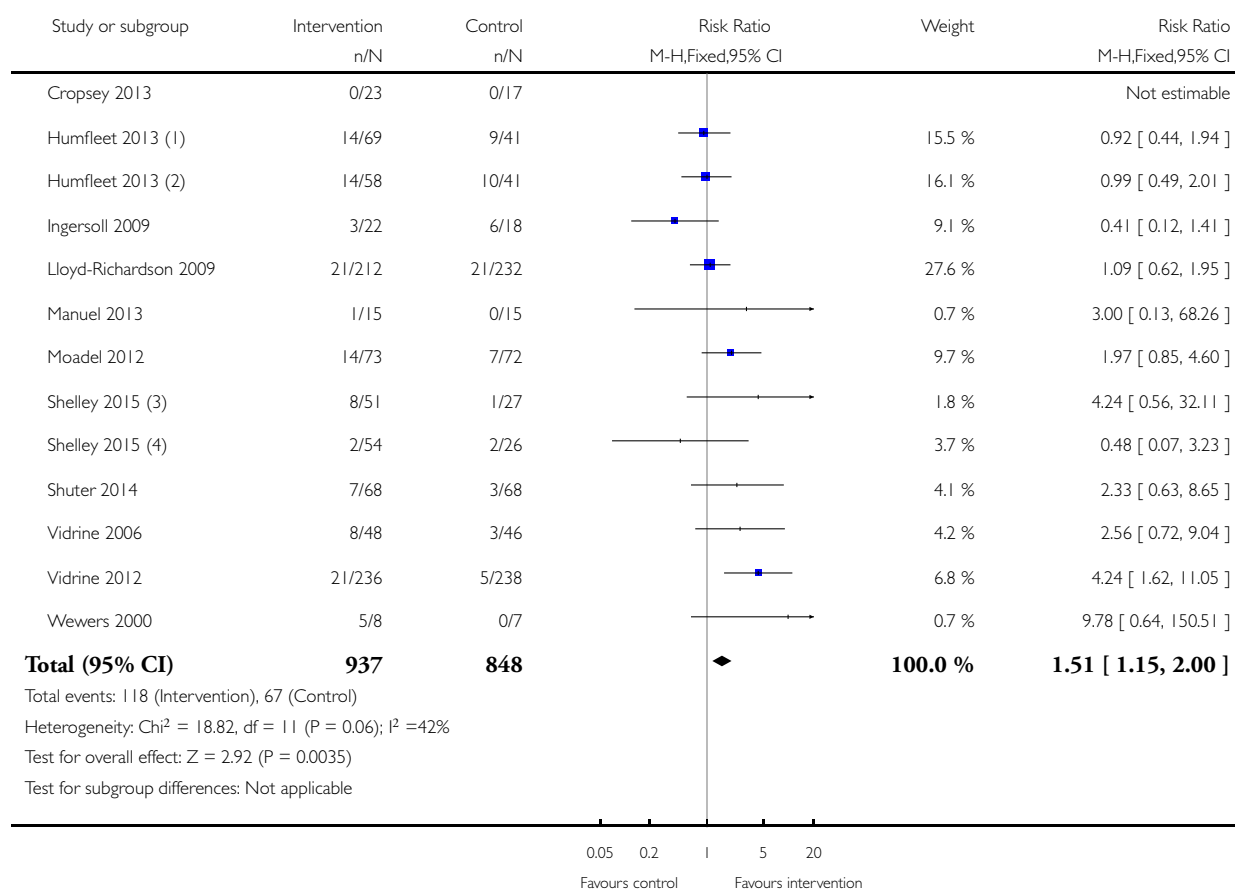
(4) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

## Analysis 2.1. Comparison 2 Tobacco cessation intervention versus control, Outcome 1 Short-term abstinence (4 weeks to < 6 months).

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 2 Tobacco cessation intervention versus control

Outcome: 1 Short-term abstinence (4 weeks to < 6 months)



(1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

(2) CBI versus Control (Control arm split between interventions to avoid double counting)

(3) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

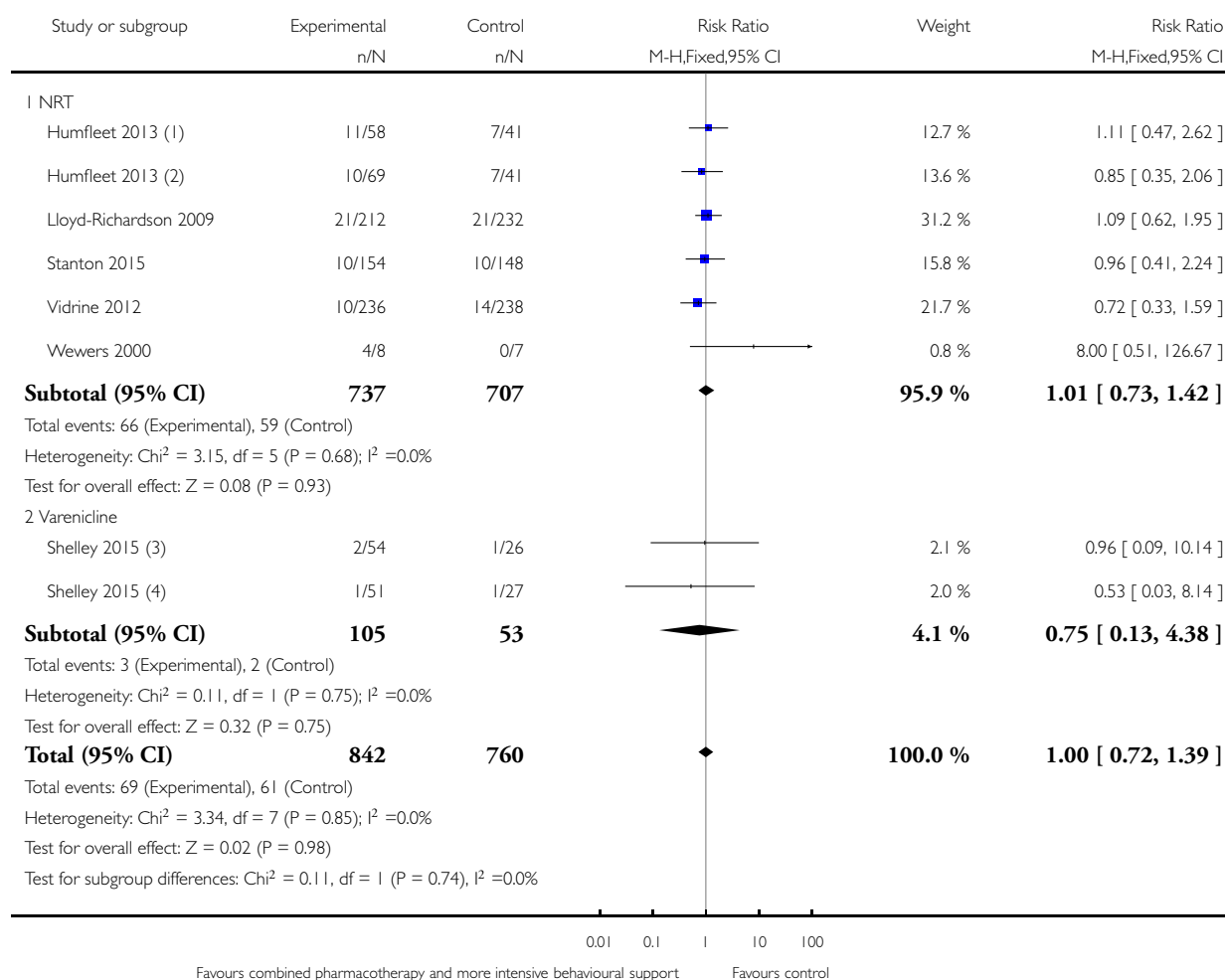
(4) Text messages versus Control (Control arm split between interventions to avoid double counting)

### Analysis 3.1. Comparison 3 Subgroup by drug, Outcome 1 Cessation at long-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 3 Subgroup by drug

Outcome: 1 Cessation at long-term follow-up



(1) CBI versus Control (Control arm split between interventions to avoid double counting)

(2) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

(3) Text messages versus Control (Control arm split between interventions to avoid double counting)

(4) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

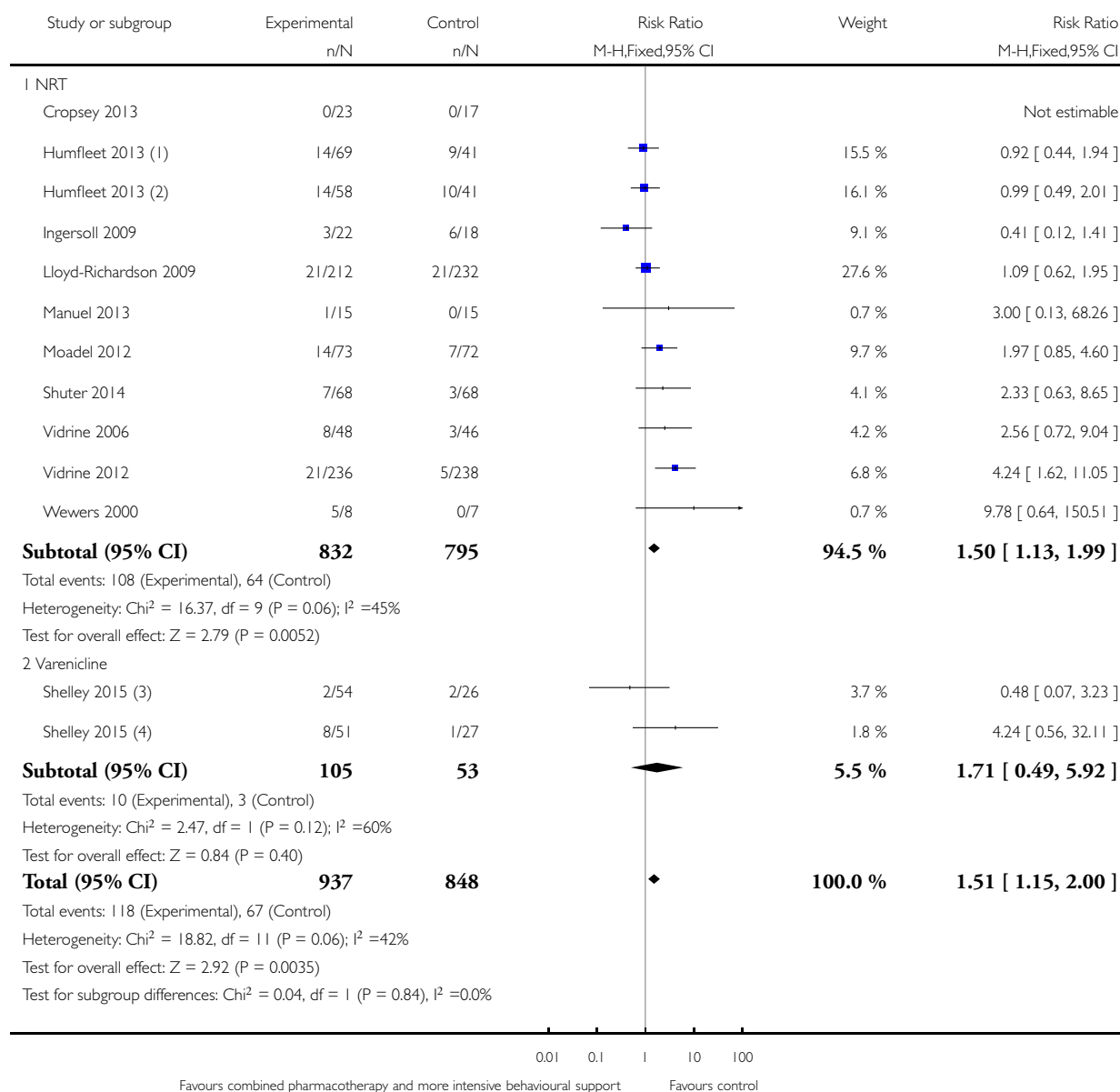


### Analysis 3.2. Comparison 3 Subgroup by drug, Outcome 2 Cessation at short-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 3 Subgroup by drug

Outcome: 2 Cessation at short-term follow-up



(1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

(2) CBI versus Control (Control arm split between interventions to avoid double counting)

(3) Text messages versus Control (Control arm split between interventions to avoid double counting)

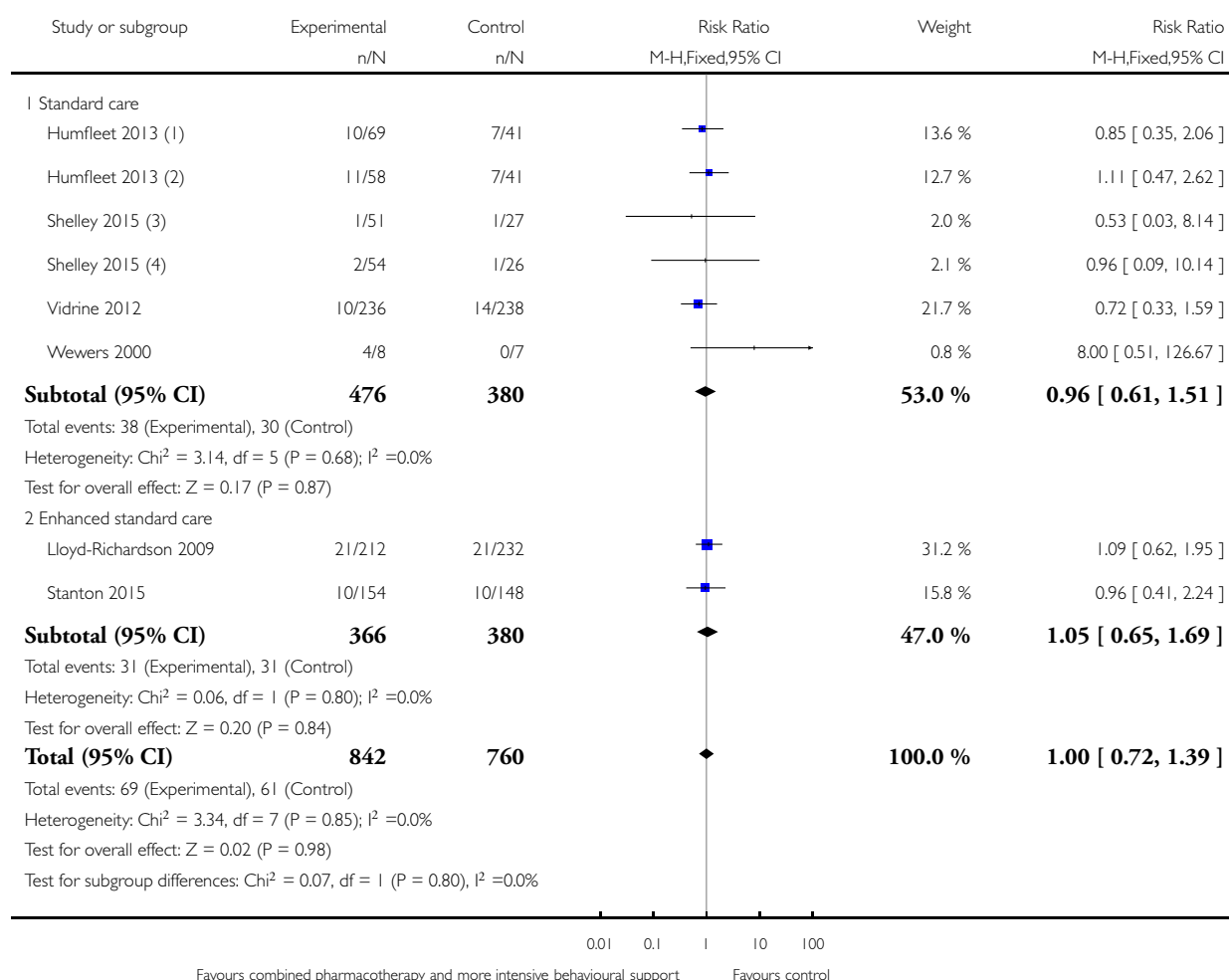
(4) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

### Analysis 4.1. Comparison 4 Subgroup by control, Outcome 1 Long-term cessation.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 4 Subgroup by control

Outcome: 1 Long-term cessation



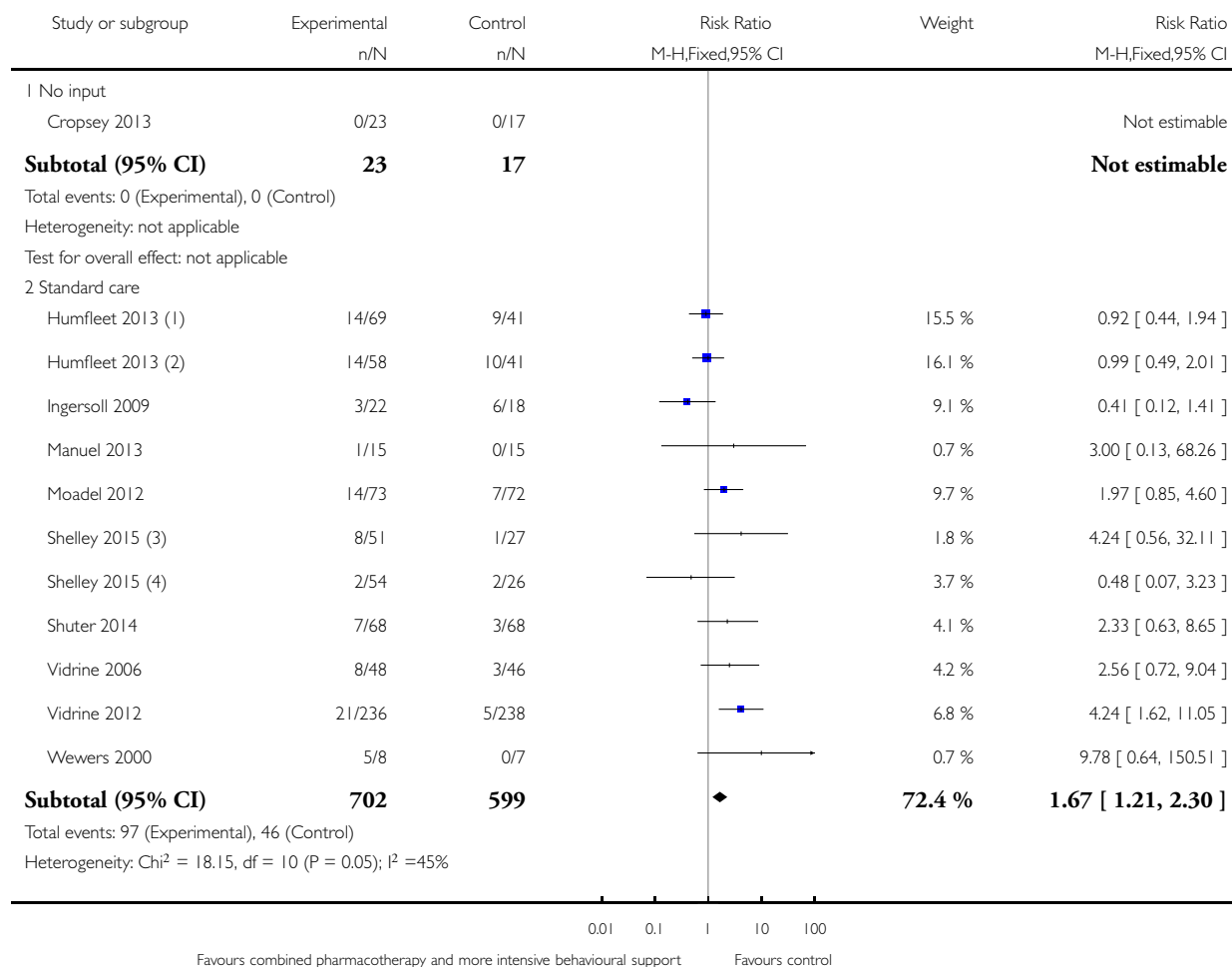
- (1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)
- (2) CBI versus Control (Control arm split between interventions to avoid double counting)
- (3) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)
- (4) Text messages versus Control (Control arm split between interventions to avoid double counting)

#### Analysis 4.2. Comparison 4 Subgroup by control, Outcome 2 Short-term cessation.

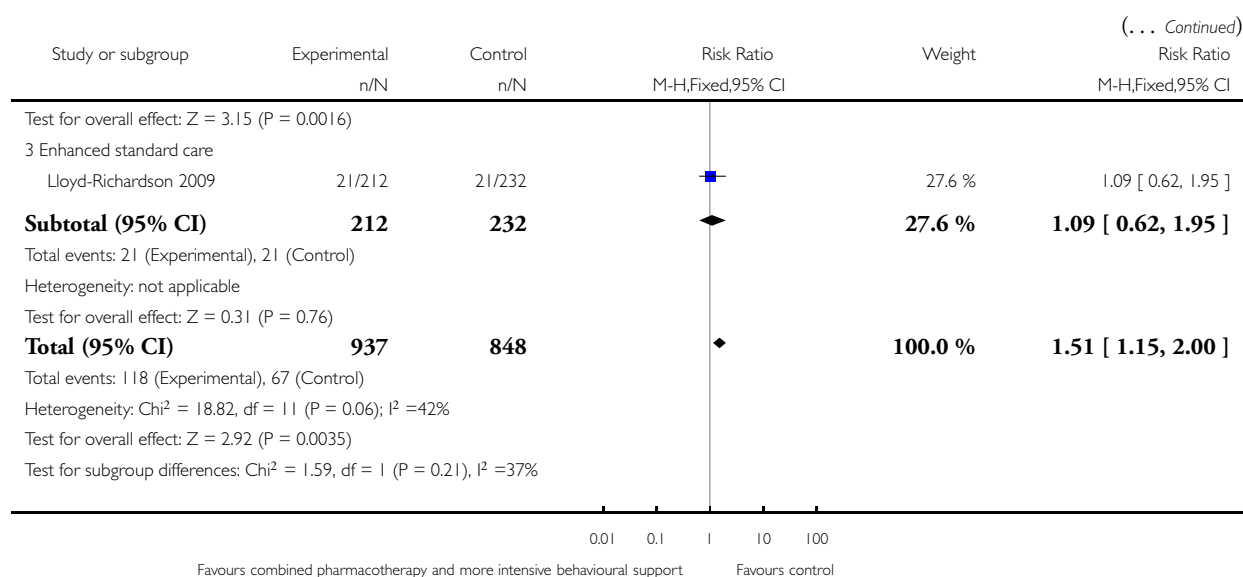
Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 4 Subgroup by control

Outcome: 2 Short-term cessation



(Continued ...)



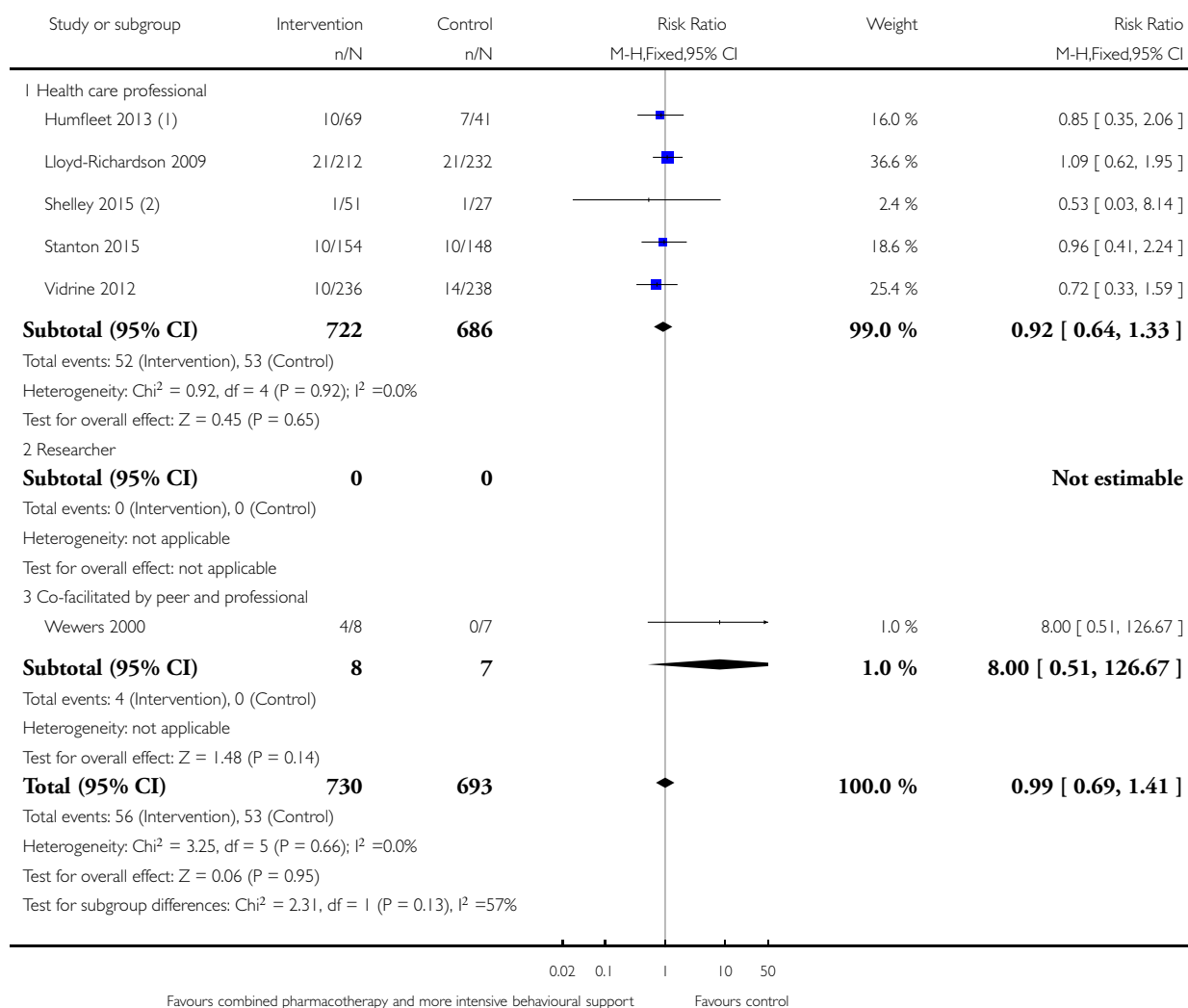
- (1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)
- (2) CBI versus Control (Control arm split between interventions to avoid double counting)
- (3) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)
- (4) Text messages versus Control (Control arm split between interventions to avoid double counting)

## Analysis 5.1. Comparison 5 Subgroup by provider, Outcome 1 Cessation at long-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 5 Subgroup by provider

Outcome: 1 Cessation at long-term follow-up



(1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

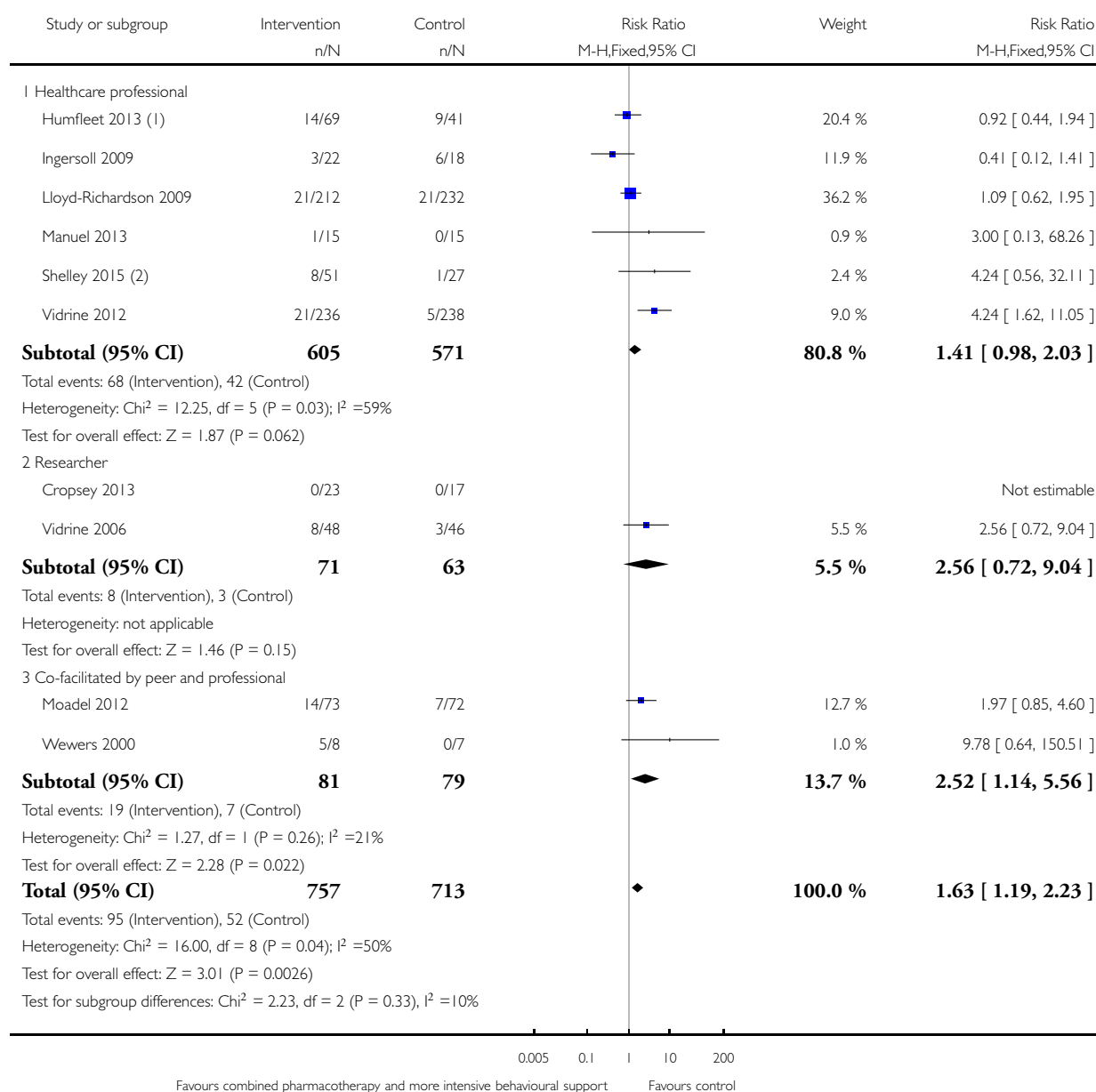
(2) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

## Analysis 5.2. Comparison 5 Subgroup by provider, Outcome 2 Cessation at short-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 5 Subgroup by provider

Outcome: 2 Cessation at short-term follow-up



(1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

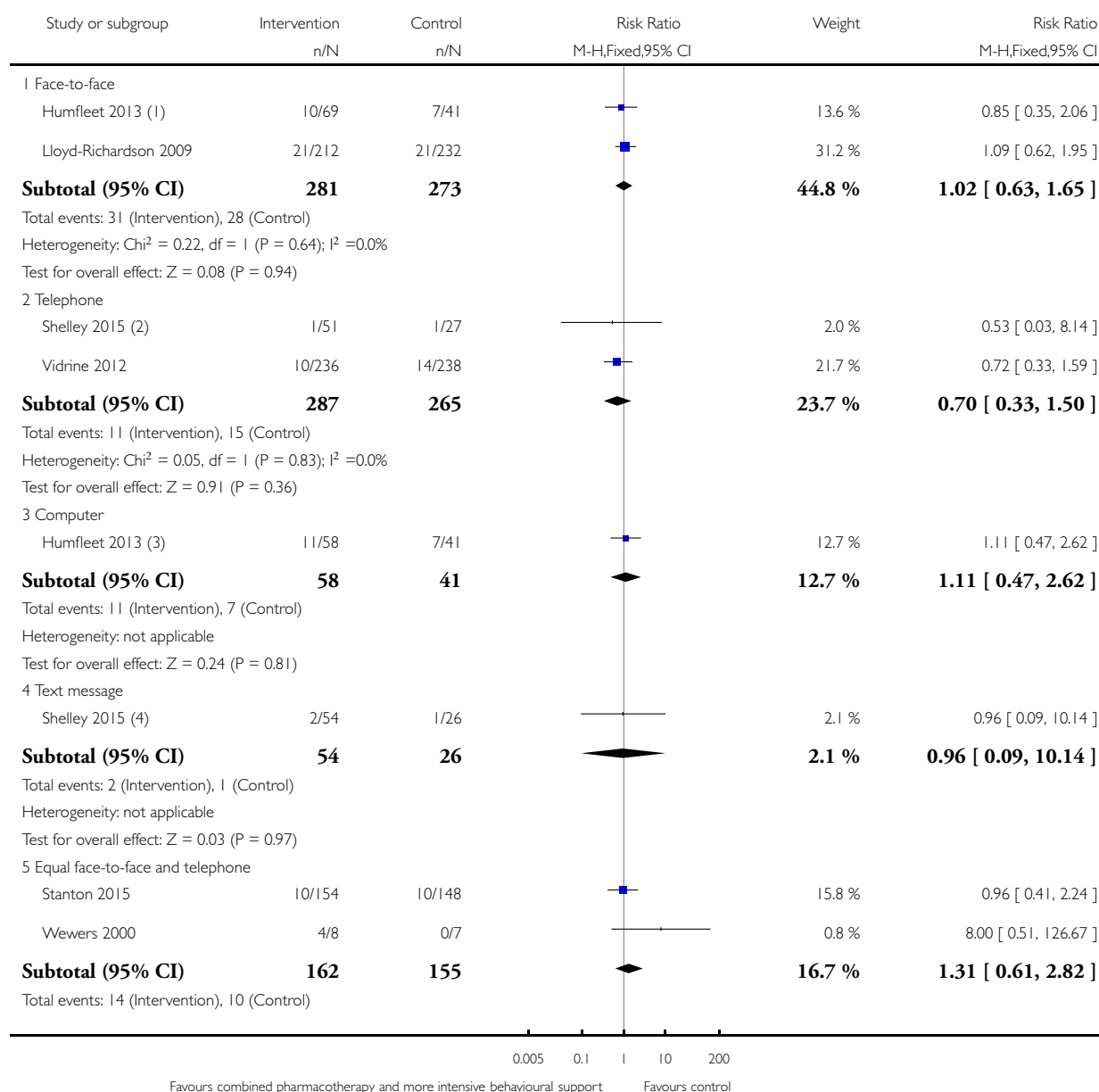
(2) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

## Analysis 6.1. Comparison 6 Subgroup by mode of contact, Outcome 1 Cessation at long-term follow-up.

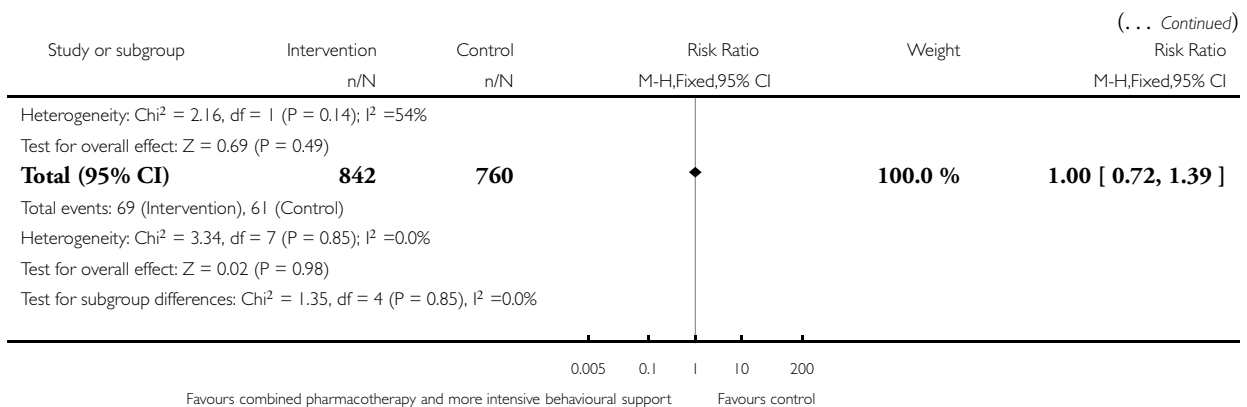
Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 6 Subgroup by mode of contact

Outcome: 1 Cessation at long-term follow-up



(Continued ...)



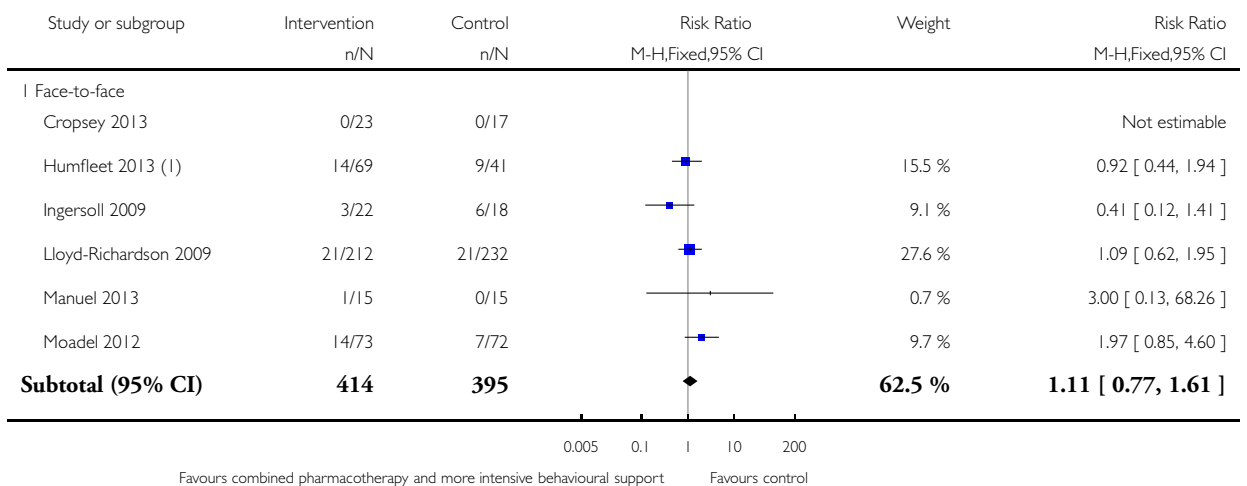
- (1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)
- (2) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)
- (3) CBI versus Control (Control arm split between interventions to avoid double counting)
- (4) Text messages versus Control (Control arm split between interventions to avoid double counting)

## Analysis 6.2. Comparison 6 Subgroup by mode of contact, Outcome 2 Cessation at short-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 6 Subgroup by mode of contact

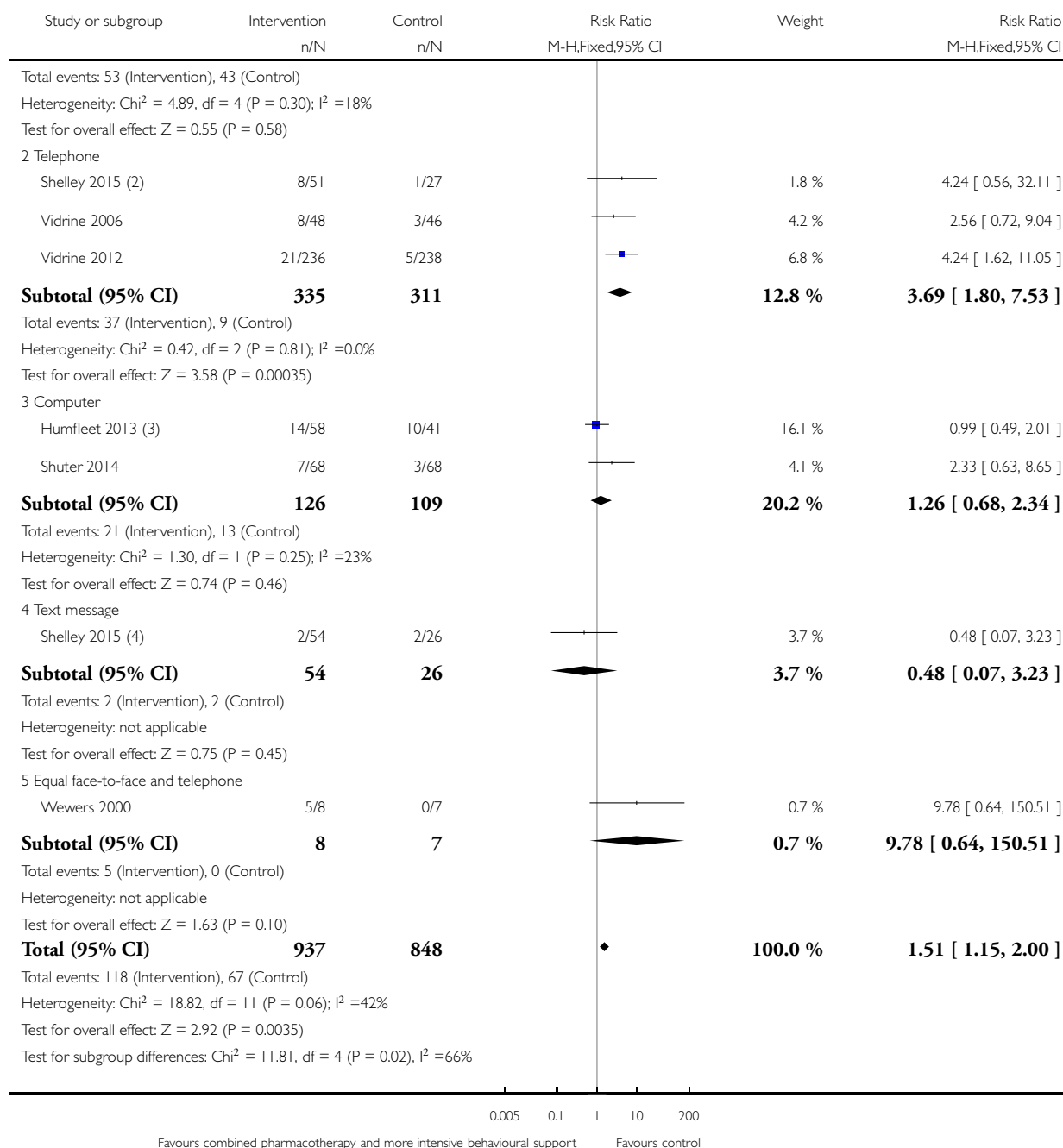
Outcome: 2 Cessation at short-term follow-up



(Continued ...)



(... Continued)



(1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

(2) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

(3) CBI versus Control (Control arm split between interventions to avoid double counting)

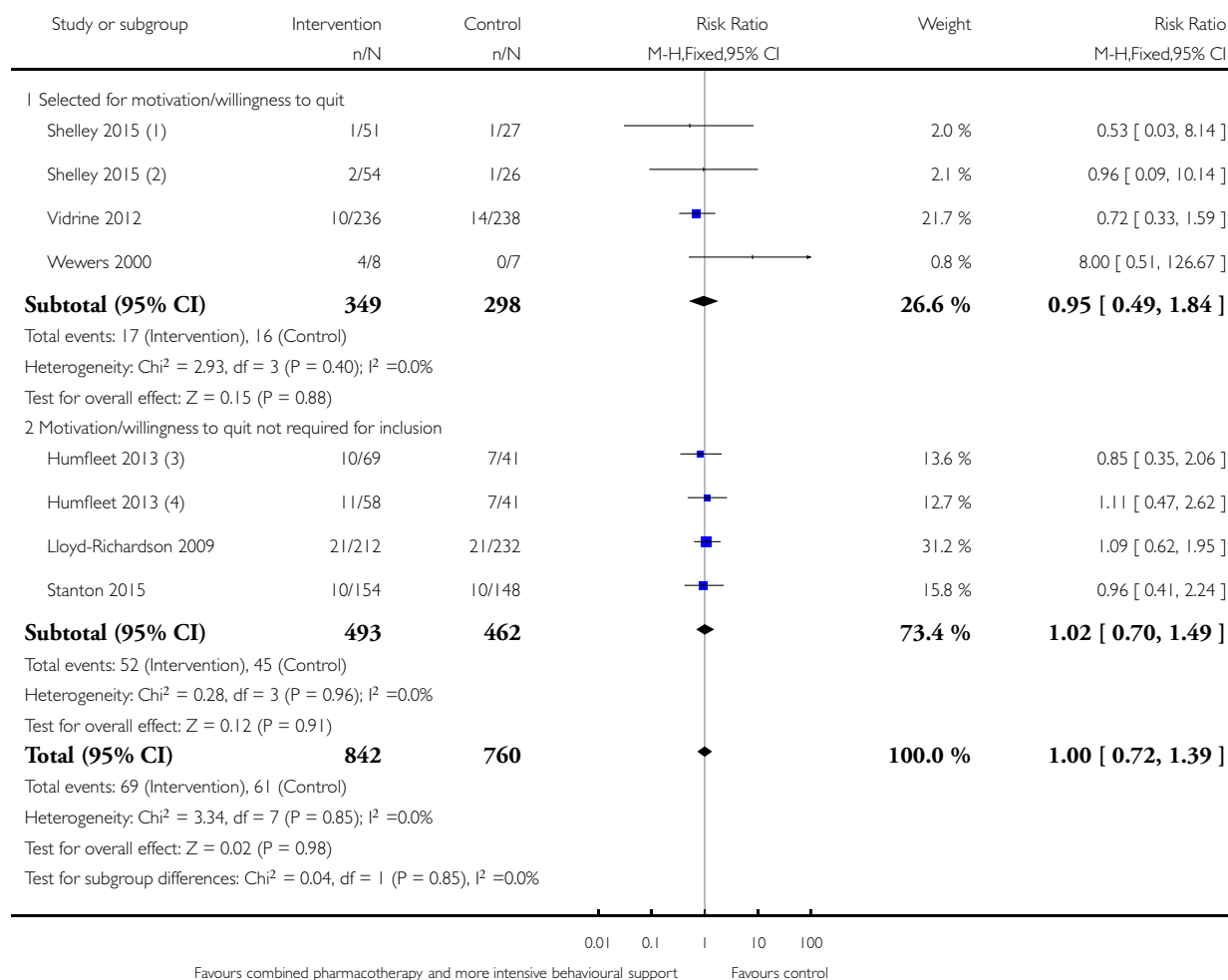
(4) Text messages versus Control (Control arm split between interventions to avoid double counting)

## Analysis 7.1. Comparison 7 Subgroup by selection, Outcome 1 Cessation at long-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 7 Subgroup by selection

Outcome: 1 Cessation at long-term follow-up



(1) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

(2) Text messages versus Control (Control arm split between interventions to avoid double counting)

(3) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

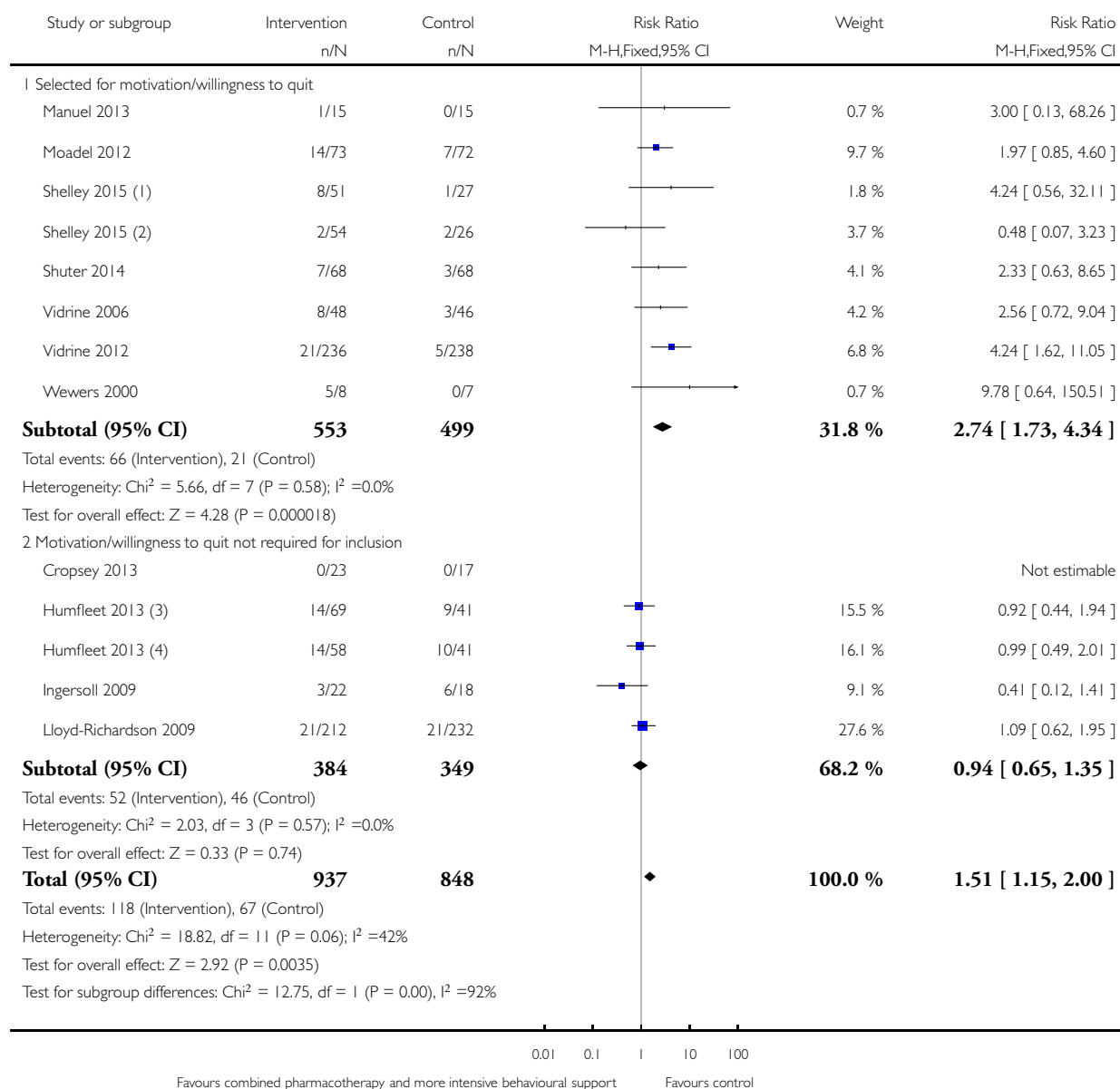
(4) CBI versus Control (Control arm split between interventions to avoid double counting)

## Analysis 7.2. Comparison 7 Subgroup by selection, Outcome 2 Cessation at short-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 7 Subgroup by selection

Outcome: 2 Cessation at short-term follow-up



(1) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

(2) Text messages versus Control (Control arm split between interventions to avoid double counting)

(3) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

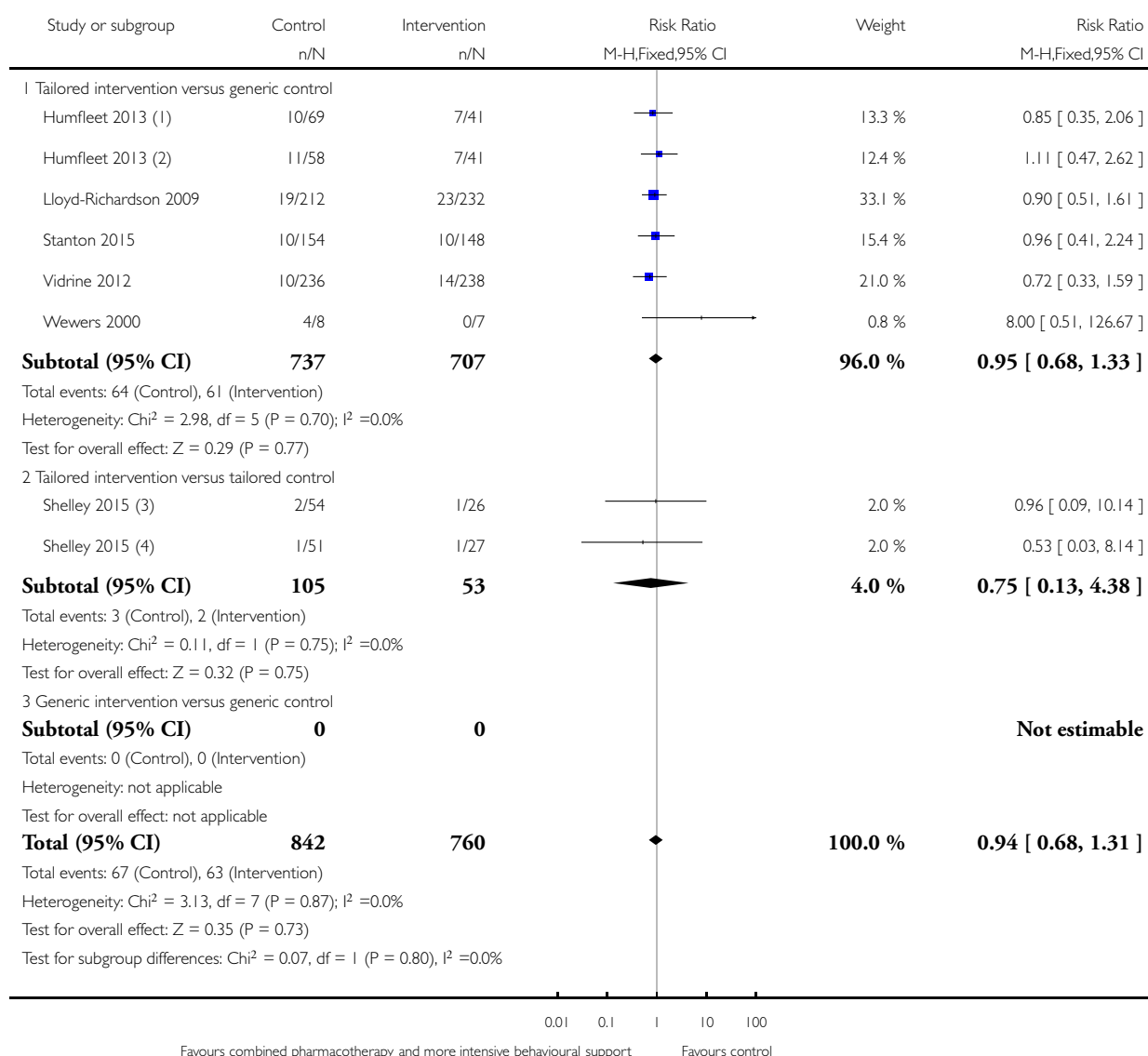
(4) CBI versus Control (Control arm split between interventions to avoid double counting)

### Analysis 8.1. Comparison 8 Subgroup by tailoring, Outcome 1 Cessation at long-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 8 Subgroup by tailoring

Outcome: 1 Cessation at long-term follow-up



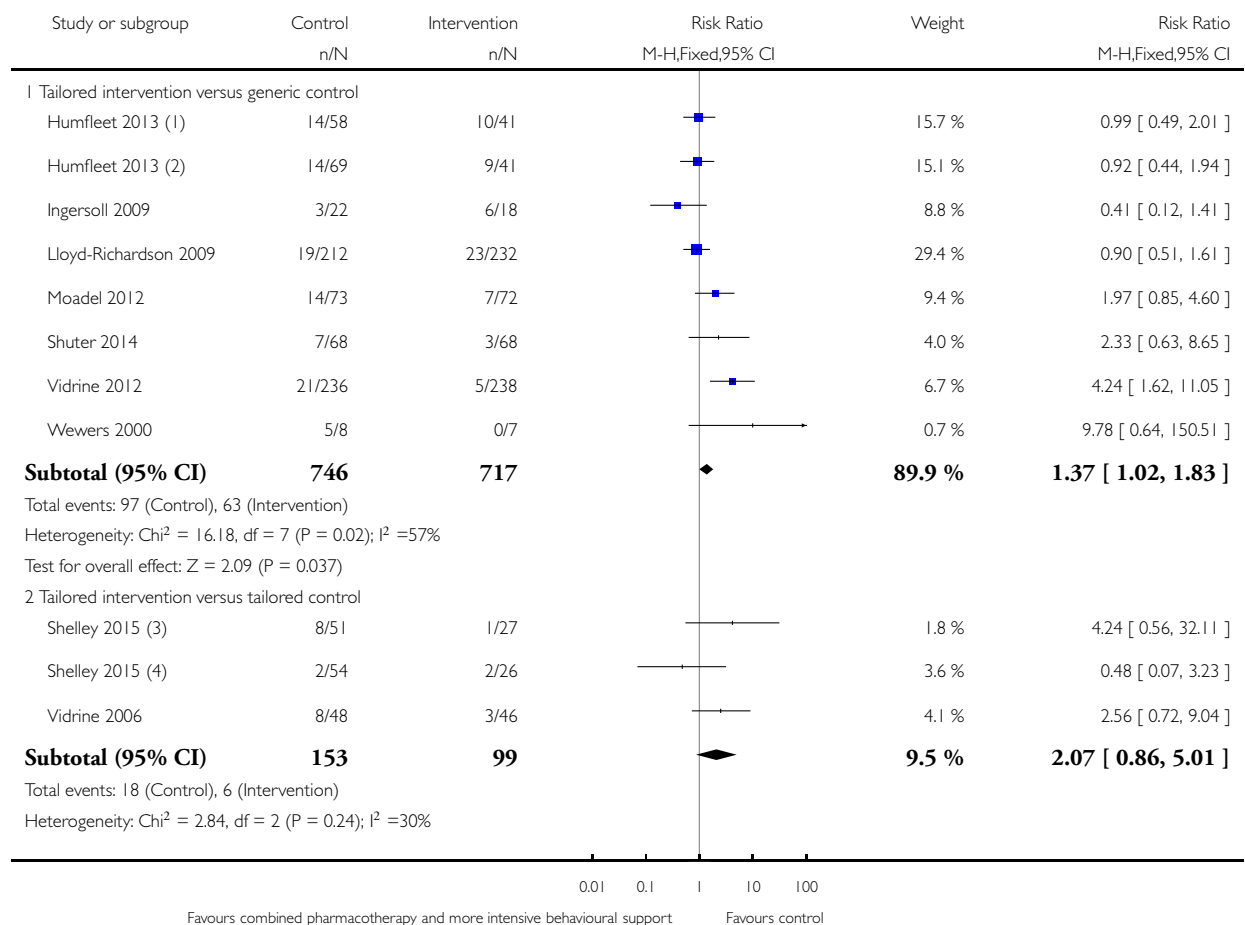
- (1) Individual counselling versus Control (Control arm split between interventions to avoid double counting)
- (2) CBI versus Control (Control arm split between interventions to avoid double counting)
- (3) Text messages versus Control (Control arm split between interventions to avoid double counting)
- (4) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

## Analysis 8.2. Comparison 8 Subgroup by tailoring, Outcome 2 Cessation at short-term follow-up.

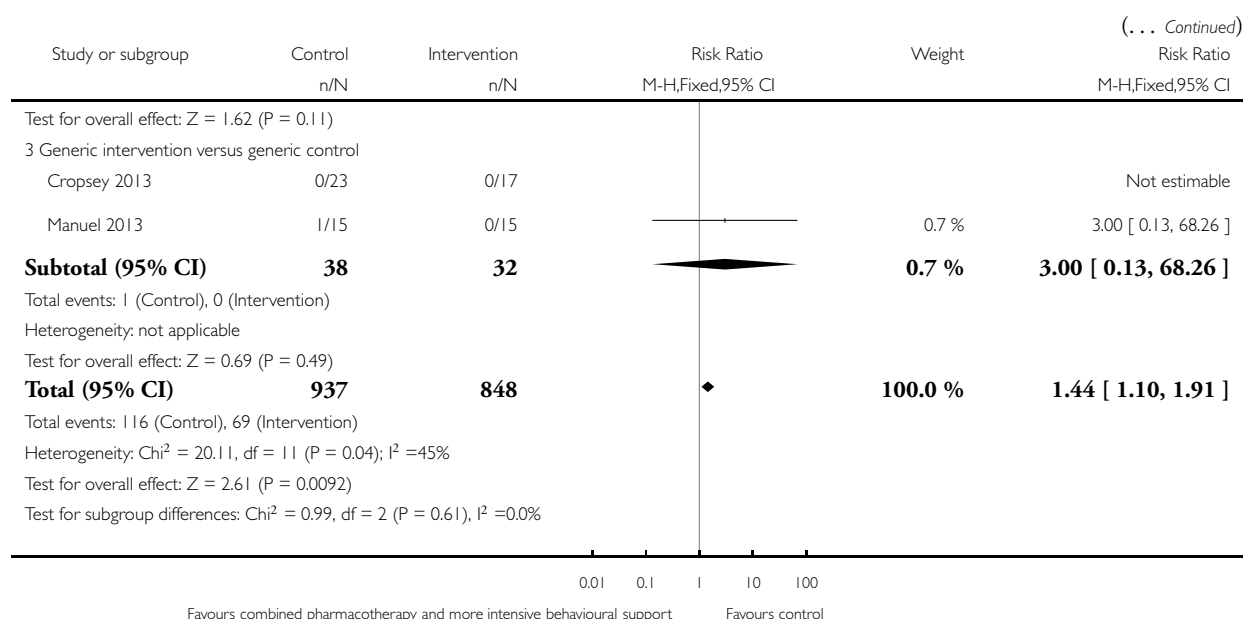
Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 8 Subgroup by tailoring

Outcome: 2 Cessation at short-term follow-up



(Continued ...)



(1) CBI versus Control (Control arm split between interventions to avoid double counting)

(2) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

(3) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

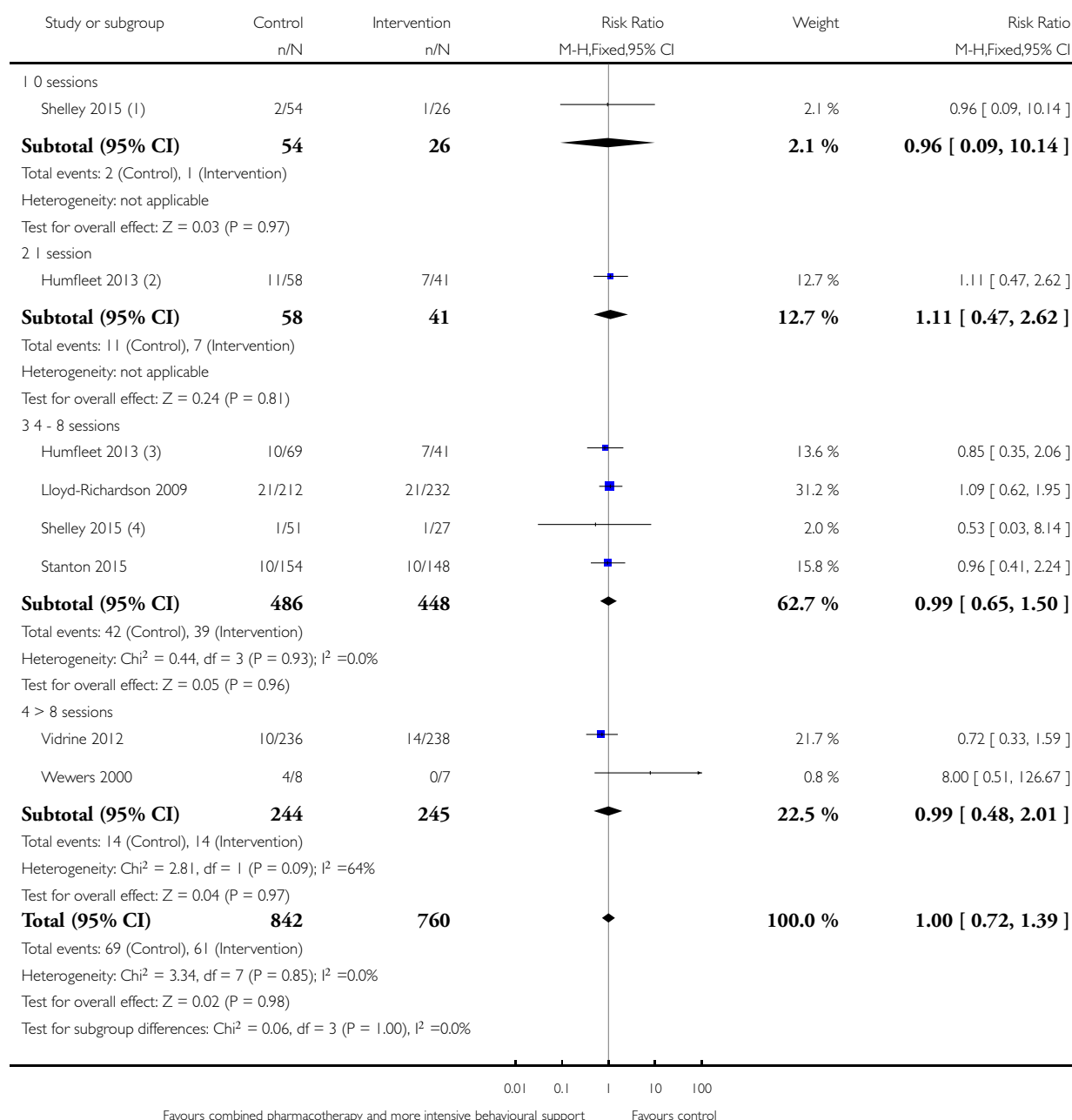
(4) Text messages versus Control (Control arm split between interventions to avoid double counting)

## Analysis 9.1. Comparison 9 Subgroup by number of sessions, Outcome 1 Cessation at long-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

Comparison: 9 Subgroup by number of sessions

Outcome: 1 Cessation at long-term follow-up



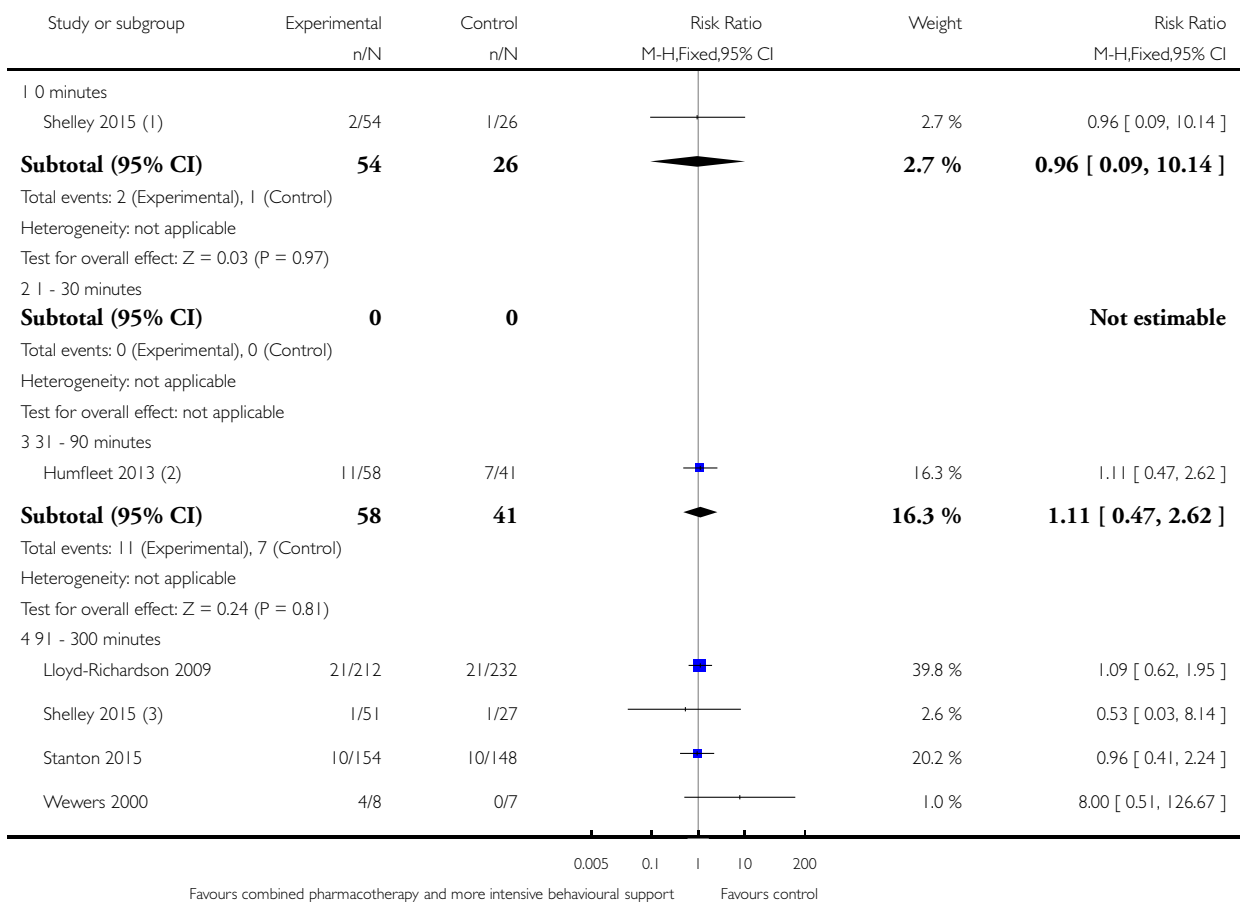
- (1) Text messages versus Control (Control arm split between interventions to avoid double counting)
- (2) CBI versus Control (Control arm split between interventions to avoid double counting)
- (3) Individual counselling versus Control (Control arm split between interventions to avoid double counting)
- (4) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

### Analysis 10.1. Comparison 10 Subgroup by total contact time, Outcome 1 Cessation at long-term follow-up.

Review: Interventions for tobacco use cessation in people living with HIV and AIDS

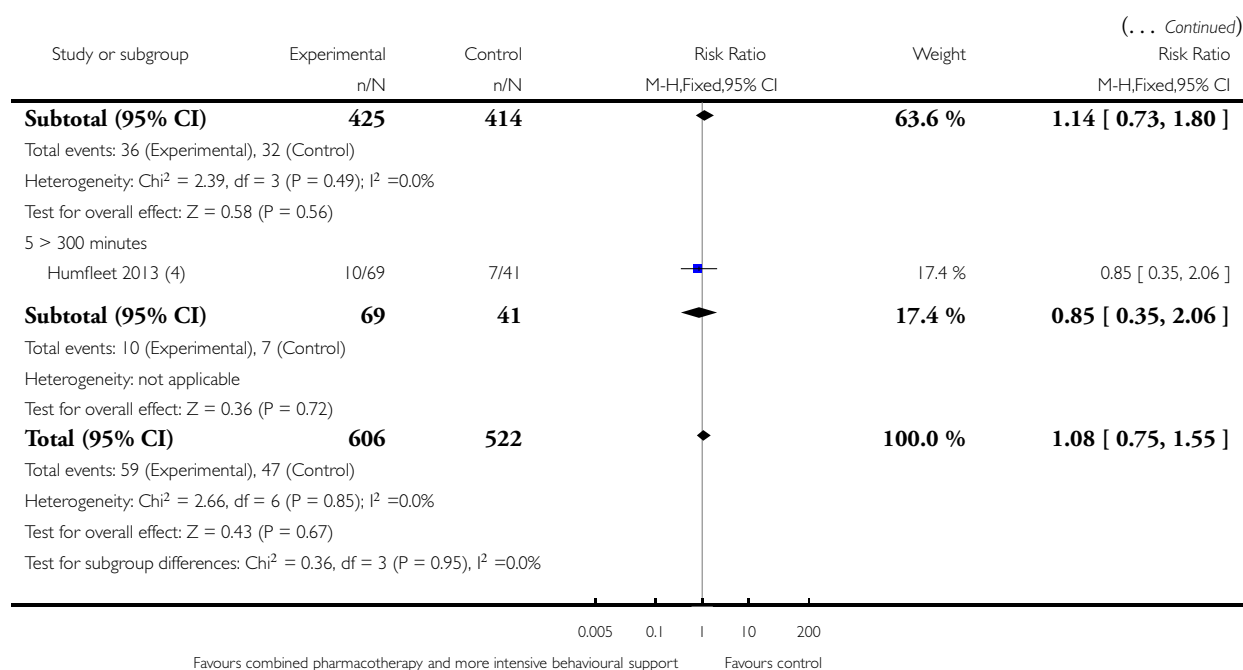
Comparison: 10 Subgroup by total contact time

Outcome: 1 Cessation at long-term follow-up



(Continued ...)





(1) Text messages versus Control (Control arm split between interventions to avoid double counting)

(2) CBI versus Control (Control arm split between interventions to avoid double counting)

(3) Adherence Behavioural Therapys versus Control (Control arm split between interventions to avoid double counting)

(4) Individual counselling versus Control (Control arm split between interventions to avoid double counting)

## APPENDICES

### Appendix I. MEDLINE search strategy

Search terms for MEDLINE search:

1. RANDOMIZED-CONTROLLED-TRIAL.pt.
2. CONTROLLED-CLINICAL-TRIAL.pt.
3. CLINICAL-TRIAL.pt.
4. Meta analysis.pt.
5. exp Clinical Trial/
6. Random-Allocation/
7. randomized-controlled trials/
8. double-blind-method/
9. single-blind-method/
10. placebos/
11. Research-Design/
12. ((clin\$ adj5 trial\$) or placebo\$ or random\$).ti,ab.

13. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj5 (blind\$ or mask\$)).ti,ab.
14. (volunteer\$ or prospectiv\$).ti,ab.
15. exp Follow-Up-Studies/
16. exp Retrospective-Studies/
17. exp Prospective-Studies/
18. exp Evaluation-Studies/ or Program-Evaluation.mp.
19. exp Cross-Sectional-Studies/
20. exp Behavior-therapy/
21. exp Health-Promotion/
22. exp Community-Health-Services/
23. exp Health-Education/
24. exp Health-Behavior/
25. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
26. smoking cessation.mp. or exp Smoking Cessation/
27. "Tobacco-Use-Cessation"/
28. "Tobacco-Use-Disorder"/
29. Tobacco-Smokeless/
30. exp Tobacco-Smoke-Pollution/
31. exp Tobacco-/
32. exp Nicotine-/
33. ((quit\$ or stop\$ or ceas\$ or giv\$) adj5 smoking).ti,ab.
34. exp Smoking/pc, th [Prevention & Control, Therapy]
35. 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 [A category smoking terms]
36. exp Smoking/ not 35 [B category smoking terms]
37. 1 or 2 or 3 [Likely CT design terms; RCTs, CCTs, Clinical trials]
38. 35 and 25 [A category smoking+all design terms]
39. 35 and 37 [A category smoking terms+likely CT design terms]
40. (animals not humans).sh. [used with 'not' to exclude animal studies for each subset]
41. ((26 or 27 or 28 or 29) and REVIEW.pt.) not 38 [Set 4: Core smoking related reviews only]
42. 36 and 25 [B category smoking+all design terms]
43. (42 and 37) not 40 [Set 3: B smoking terms, likely CT design terms, human only]
44. 38 not 39 not 40 [Set 2: A smoking terms, not core CT terms, human only]
45. (35 and 37) not 40 [Set 1: A smoking terms, likely CT design terms, human only]
46. exp Smoking Cessation/ not (44 or 45) [Smoking cessation only, no design terms]
47. exp hiv infections/ or exp acquired immunodeficiency syndrome/
48. hiv/ or hiv-1/ or hiv-2/
49. ("acquired immunodeficiency syndrome" or "acquired immunedeficiency syndrome" or "acquired immuno-deficiency syndrome" or "acquired immune-deficiency syndrome").mp.
50. "HIV/AIDS".mp.
51. HIV.mp.
52. PLWHA.mp
53. 47 or 48 or 49 or 50 or 51 or 52 [Any topic term]
54. 45 and 53 [Set 1 plus topic]
55. 44 and 53 [Set 2 plus topic]
56. 43 and 53 [Set 3 plus topic]
57. 54 or 55 or 56 [All sets]

## CONTRIBUTIONS OF AUTHORS

Erica Pool (EP) and Kamran Siddiqi (KS) conceived the review. EP wrote the protocol, with input from KS and Omara Dogar (OD). EP, KS and Ryan Lindsay (RL) screened the reports and agreed on inclusion of the studies. EP, RL, and OD extracted data. EP drafted the text. EP undertook the analyses, with input from OD. KS and Peter Weatherburn (PW) provided overall supervision of the project. All authors reviewed the text and are responsible for the analyses and conclusions.

## DECLARATIONS OF INTEREST

Erica Pool (EP), Omara Dogar (OD), Ryan Lindsay (RL), and Peter Weatherburn (PW) have no conflicts of interest to declare.

Kamran Siddiqi (KS) has received a research grant (GRAND 2014) from Pfizer, a pharmaceutical company that makes drugs for tobacco cessation.

## SOURCES OF SUPPORT

### Internal sources

- London School of Hygiene and Tropical Medicine, UK.

This review was partly undertaken during Erica Pool's study at the London School of Hygiene and Tropical Medicine, which was supported by the LSHTM UK/EU Studentship Award.

- NIHR Academic Clinical Fellowship, UK.

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### External sources

- No sources of support supplied

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We could not address one of the secondary objectives - to assess whether interventions combining pharmacotherapy and behavioural support are more effective than either type of support alone in PLWHA - due to all included studies providing a combined intervention. We added a post hoc objective - to assess whether more intense behavioural support is more effective. This involved analysis according to number of sessions and total duration of contact time.

We were unable to perform the planned synthesis of adverse events or HIV outcomes (CD4 count, viral load or incidence of opportunistic infections), since they were not reported in more than one study.

Two new authors (RL and PW) joined the review team following the protocol.

## INDEX TERMS

### Medical Subject Headings (MeSH)

\*Acquired Immunodeficiency Syndrome; \*HIV Infections; Behavior Therapy [methods]; Nicotinic Agonists [therapeutic use]; Randomized Controlled Trials as Topic; Smoking Cessation [methods]; Time Factors; Tobacco Use Cessation [\*methods]; Varenicline [therapeutic use]

### MeSH check words

Humans